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Lost in Transition: Pre-antiretroviral Care and Delayed Initiation of Antiretroviral Therapy in Uganda

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The front cover pictures: Top left is a clinic of one of the prominent traditional healers in eastern Uganda, top right is shrine belonging to a spiritual healer in Iganga. These are providers where some peopole living with HIV seek care before seeking formal care from the public facilities like the one at the bottom

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ABSTRACT

Background: Comprehensive HIV care aims at providing care and support, from HIV counselling and testing, through pre-antiretroviral (pre-ARV) care to antiretroviral therapy (ART). However, many people living with HIV (PLHIV) do not start treatment or are lost to follow-up during pre-ARV care, and subsequently initiate ART very late, with a high risk of HIV/AIDS-related mortality. Determinants of uptake/retention of PLHIV under pre-ARV care and delayed ART initiation in Uganda, where HIV and ART awareness are presumably high, are not sufficiently understood.

Main aim: To investigate uptake and loss to follow-up of PLHIV under pre-ARV care and delayed ART initiation in order to inform policy and strategic planning for improved comprehensive HIV/AIDS care.

Methods: Four studies (I-IV) were conducted in Iganga district, eastern Uganda. Study I used key informant interviews (KIIs) with five health workers and 10 in-depth interviews (IDIs) with PLHIV, as well as six focus group discussions (FGDs) with caretakers of the PLHIV to explore reasons for loss to follow-up under pre-ARV care. Study II was a randomised controlled trial involving 400 participants, to evaluate the effect of extended counselling on uptake of pre-ARV care. Study III used 20 IDIs with clients on ART and 10 FGDs with caretakers of ART clients to understand reasons for delayed ART initiation. Study IV was a case-control study involving 152 cases (clients who initiated ART at CD4 < 50 cells/µl) and 202 controls (clients who initiated ART at CD4 50-200 cells/µl) to assess risk factors for very late initiation of ART. Content analysis was used for qualitative data, and univariate, bivariate and multivariate analysis for quantitative data.

Results: Reasons for dropping out of pre-ARV care included inadequate post-test counselling to PLHIV and competition from traditional/spiritual healers. Other reasons included transportation costs, long waiting time, lack of incentives to seek pre-ARV care by PLHIV who perceived themselves to be healthy, and gender inequality (I). PLHIV who underwent counselling by staff trained in basic counselling skills, combined with home visits by community network support agents, were 1.8 times more likely to take up pre-ARV care compared to PLHIV who received the standard care (RR 1.8; 95% CI 1.4-

2.1) (II). ARV stock-outs, inadequate pre-ARV care and perceived lack of staff confidentiality were system barriers to timely ART initiation. Weak family/social support and misconceptions about ARVs were cited as individual/community barriers to timely ART initiation (III). Seeking care from traditional/spiritual healers before attending formal care (AOR 7.8; 95% CI 3.7-16.4), lack of pre-ARV care (AOR 4.6; 95% CI 2.3-9.3), subsistence farming (AOR 6.3; 95% CI 3.1-13.0) and lack of family/social support (AOR 3.3; 95% CI 1.6-6.6) were crucial risk factors for very late ART initiation (IV). Higher age (AOR 0.9; 95% CI 0.8-0.9) and being female (AOR 0.4; 95% CI 0.2-0.8) were protective factors against very late initiation of ART (IV).

Discussion: Adequate post-test counselling for newly diagnosed PLHIV, combined with follow-up care by network support agents, could help retain PLHIV under pre-ARV care and allow timely initiation of ART. Trained and supervised traditional/spiritual healers could complement government efforts in offering some components of pre-ARV care. ART services should be made more affordable, accessible and user-friendly to enhance timely ART initiation. Other system deficiencies, such as stock-outs of cotrimoxazole and ARVs and lack of adequate staff also need to be addressed. There is a need for social mobilisation to address gender inequality, stigma and misconceptions about ARVs and to boost social support for PLHIV.

Key words: counselling, community support agents, pre-ARV care, traditional/spiritual healers, HIV, antiretroviral treatment, adherence, Uganda

LIST OF PUBLICATIONS

I **Muhamadi Lubega**, Xavier Nsabagasani, Tumwesigye Nazarius Mbona, Fred Wabwire-Mangen, Anna Mia Ekström, George Pariyo, Stefan Peterson. (2010) Policy and practice, lost in transition: Reasons for high drop-out from pre-antiretroviral care in a resource-poor setting of eastern Uganda. *Health Policy* 95: 153-158.

II **Muhamadi Lubega**, Tumwesigye Nazarius Mbona, Daniel Kadobera, Gaetano Marrone, Fred Wabwire-Mangen, George Pariyo, Stefan Peterson, Anna Mia Ekström. A Single-blind Randomized Controlled Trial to evaluate the effect of Extended Counseling on Uptake of Pre-antiretroviral care in Eastern Uganda (Submitted).

III **Muhamadi Lubega**, Xavier Nsabagasani, Tumwesigye Nazarius Mbona, Fred Wabwire-Mangen, Anna Mia Ekström, Stefan Peterson, George Pariyo. (2010) Inadequate pre-antiretroviral care, stock-out of antiretroviral drugs and stigma: Policy challenges/bottlenecks to the new WHO recommendations for earlier initiation of antiretroviral therapy (CD < 350 cells/µL) in eastern Uganda. *Health Policy* 97: 187-194.

IV **Muhamadi Lubega**, Tumwesigye Nazarius Mbona, Daniel Kadobera, Gaetano Marrone, Fred Wabwire-Mangen, George Pariyo, Stefan Peterson, Anna Mia Ekström. Lack of pre-antiretroviral care and competition from traditional healers, crucial risk factors for very late initiation of antiretroviral therapy for HIV - A case-control study from eastern Uganda.*The Pan African Medical Journal (PAMJ)* Vol 8, Number 40, 2011.

The above papers/studies will be referred to by their Roman numerals I - IV.

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LIST OF ABBREVIATIONS

AOR	Adjusted odds ratio
ART	Antiretroviral therapy
ARV	Anti-retroviral drugs
CI	Confidence interval
HCT	HIV counselling and testing
HIV	Human immunodeficiency virus
MDG	Millennium Development Goal
MOH	Ministry of Health
NGOs	Non-governmental organisations
OR	Odds ratio
PIHCT	Provider-initiated counselling and testing
PLHIV	People living with HIV/AIDS
PMTCT	Prevention of mother-to-child transmission
Pre-ARV	Pre-antiretroviral
RCT	Randomised controlled trial
RR	Risk ratio
SEM	Socio ecological model
SSA	Sub-Saharan Africa
UAC	Uganda Aids Commission
UBOS	Uganda Bureau of Statistics
VCT	Voluntary counselling and testing
WHO	World Health Organisation

PREFACE

"Ondekeire abaana musengwa wange, singa wajja wanhwaku obulezi bwataso, tomanha walibaierewo" (You have left me with orphans my boss, if you had gone for treatment from the AIDS support organisation, maybe you would still be alive).

This was the cry I heard from a middle-aged woman at the clinician's office in the outpatients' section when conducting an evening hospital round as Medical Superintendent of Iganga Hospital way back in 2006. The hospital was constructed in 1968 and is located 115 km east of the capital of Uganda, Kampala. Time check was 8.00 pm. The woman's cry had attracted many people around the department. Outside the department was a motorcycle they had hired to bring the patient to the hospital from their home 50 km away.

Inside the clinician's office lay the body of a young man on a stretcher; he had clear signs of severe wasting. I looked straight into the clinician's face. He looked sad and resigned. This same clinician also worked in the antiretroviral therapy (ART) clinic. He informed me that he vividly remembered having attended to the deceased some years back, in the pre-antiretroviral (pre-ARV) clinic, but that the deceased had most likely not returned for care since then.

By the body sat an elderly woman, who I later found out was the mother of the deceased. With many reflections, I looked outside the window, and my eyes met a mixture of darkness and stars. I calmed the woman and talked to her, only to confirm that indeed the deceased had tested HIV-positive at Iganga Hospital years back, but chose to seek spiritual healing until this fateful day, when the pastor told them to go to hospital because the patient had been convulsing the whole day. I instructed the hospital administrator to organise some transport for the deceased to the burial site.

As I drove back home, I wondered whether there was something we could have done earlier to follow-up this patient before this fateful day. The following morning, I invited the person in charge of the ART clinic for a chat. After a brief discussion and review of the pre-ART register, I realised that this was not an isolated case. Indeed, approximately 90% of the clients who were supposed to attend the pre-ARV clinic regularly had been lost to follow-up. This stimulated my

interest in looking at the ART register, only to discover that many of our clients in the ART clinic were cases of late diagnosis who had initiated ART when they had very low CD4 cell counts. These particular patients had not been attending the pre-ARV clinic either, but were coincidentally diagnosed through provider-initiated HIV counselling and testing on suspicion of AIDS.

How, as overall supervisor of services at the facility, could I have allowed this to happen? I contemplatively looked outside the window of my office and convinced myself that it was not time to lament and blame anyone. The question in my mind was what can be done to ensure that people who test HIV-positive are regularly followed up so that they initiate ART on time?
My efforts to contribute to answering this question is the focus of this thesis.

1.0 INTRODUCTION

1.1 The HIV pandemic

Globally the number of people living with HIV/AIDS (PLHIV) is estimated at 33.3 million people (31.4 - 35.3 million). Of these, 30.8 million are adults (15-45 years) and 2.5 million are children under 15 years of age. Women account for approximately 52% of the adult population living with HIV/AIDS. In 2009 the total number of people newly infected with HIV was approximately 2.6 million. By the end of 2009 sub-Saharan Africa (SSA), which has only 10% of the total global population, accounted for 22.5 million (68%) of all people living with HIV (PLHIV), 72% of AIDS deaths and 70% of all the new infections worldwide (UNAIDS, 2010).

The pandemic is impeding economic development and has dramatically decreased the life expectancy in several African countries. It has also over-stretched the already weak health care systems in many resource-poor settings. HIV/AIDS is now well established on the list of the top five leading causes of death worldwide, and is responsible for one in every five deaths in SSA (Kumarasamy *et al*., 2007; UNAIDS, 2008a; World Health Organisation (WHO), 2003b; Piot *et al*., 2001; UNAIDS, 2010).

The global response to the HIV pandemic includes prioritising HIV care among the Millennium Development Goals (MDGs 6a and b) adopted by world leaders in the year 2000. The sixth MDG aims to provide access to antiretroviral therapy (ART) to 50% of all those who need it and to have halted and begun to reverse the spread of HIV by 2015 (UNDP, 2010, UNDP, 2005). However, meeting this target, requires an effective and comprehensive HIV/AIDS response tailored to ensure universal access to HIV testing, prevention, care, treatment and support to PLHIV and their communities. The response therefore calls for a need to scale up HIV testing in order to identify all those in need of HIV treatment, and to strengthen the link between HIV diagnosis and comprehensive HIV/AIDS care, including timely initiation of ART.

Although there has been an increase in access to voluntary counselling and testing (VCT) in SSA, only 10% of the adult population know their HIV sero status, leaving a high unmet need for HIV testing (UNAIDS, 2008). Most PLHIV in SSA remain undiagnosed and cannot therefore be linked to adequate prevention, treatment, care and support (UNAIDS, 2008b; Nakanjako *et al.*,

2009). Even among those screened for HIV, however, many either do not take up comprehensive HIV care or get lost to follow-up in transition from testing HIV positive through pre-antiretroviral (pre-ARV) care to initiation of antiretroviral therapy (ART).

The international standard aims at ongoing counselling and regular pre-ARV care for newly screened PLHIV at least once every six months (for WHO stage 1 and 2) if they have no complications. With the advent of cotrimoxazole prophylaxis to prevent opportunistic infections like *Pneumocystis carinii* pneumonia and others, however, the guidelines propose quarterly monitoring of PLHIV not yet eligible for ART if no clinical problems occur and they are taking the drugs correctly (WHO, 2006; Medscape, 2008; Wendo, 2005; Minstry of Health (MOH), 2005a, 2006a). Regular pre-ARV care ensures that PLHIV are monitored to, among others, initiate ART on time. Available evidence indicates that regular pre-ARV care increases by three times the chances of initiating ART on time, with an average of 15 life years saved for those on treatment in the long run (MOH, 2004; Hallett *et al*., 2008; Nakanjako *et al*., 2009; UNAIDS, 2009).

Unfortunately, even in high-income countries up to 30% of PLHIV present late for HIV care, do not therefore benefit from the important regular pre-ARV care, and subsequently initiate ART late with a high risk of mortality. This proportion is higher in low-income countries with weaker health systems (Battegay *et al*., 2008; Nakanjako *et al*., 2009; Smart, 2007b). In SSA up to 59% of PLHIV do not enrol or adhere to the continuum of comprehensive HIV care from VCT to pre-ARV care to ART. Subsequently many PLHIV are not regularly monitored and initiate ART very late with a high risk of premature mortality (Long, 2008; Losina *et al.*, 2010; Larson *et al.*, 2010; Larsson *et al.*, 2009; Tsague, 2008).

Uganda has been heralded as a success story in the fight against HIV/AIDS, with apparently high HIV and ART awareness. The country has steered a course of a rapid increase of accredited sites offering ART, from 48 to 398 sites between 2003 and 2010 (Uganda AIDS Commission (UAC), 2007; UAC, 2010b; UNAIDS, 2008a). However, the country still suffers with a low uptake and retention rate of PLHIV under pre-ARV care, and a large proportion of PLHIV initiating ART

very late (at CD4 counts below 50 cells/µl) with a much higher risk of early mortality (Lutalo *et al*., 2009; Smart, 2007b; Hammer *et al*., 2008; Kigozi *et al.*, 2009a; UAC, 2008).

Low uptake or loss to follow-up of newly screened PLHIV under pre-ARV care and delayed ART initiation are major challenges to scaling up access to comprehensive HIV care, especially when global efforts are being driven towards earlier ART initiation, already at a CD4 count of < 350 cells/µl (Hammer *et al*., 2008; WHO, 2009b; WHO, 2009a).

1.2 Country profile of Uganda

Uganda has a projected population of 30.7 million people and an annual population growth rate of 3.3%. The under-five mortality rate is currently 137 deaths per 1000 live births, while the infant mortality rate is 75/1000 live births. The maternal mortality ratio currently stands at 435/100 000 live births (MOH, 2009) (Table 1).

Table 1. Trends of selected socio-demographic and health indicators in Uganda.

Indicator	**2002**	**2007**	**2009**
Population, total (millions)	24.2	28.4	30.7
Population growth (annual %)	3.2	3.3	3.3
Maternal mortality ratio (/100 000 live births)	505	435	435
Infant mortality rate (/1000 live births)	88	76	76
Adolescent pregnancy (%)	32	25	137
ANC attendance (four visits, %)	42	47	47
Deliveries by skilled attendant (%)	38	41	42
Contraceptive prevalence rate (%)	22.8	23.7	24
Unmet need for contraception	35	41	41
Total fertility rate	6.9	6.7	6.3
Literacy rate (%)	65	69	75
Life expectancy	51	51	53
Population below poverty line, < US$1 (%)	38	31	31
Fully immunized	38	46	64
No. of people living with HIV/AIDS	600 000	1 101 317	1 200 000
HIV prevalence (%)	6.1	6.4	6.5
New HIV infections	-	110 694	120 000
AIDS deaths	78 000	61 306	64 000
Total need for ART	75 000	322 819	379 551
Total receiving ART	-	153 718	220 139

Source: UBOS, 2007/10; UNFPA, 2008/9; UNDP, 2009; MOH, 2010;UNICEF, 2010.

Approximately 1.2 million people in Uganda are HIV-infected. Women, urban dwellers and residents of the post-conflict northern Uganda region are disproportionately affected. Sexual transmission continues to contribute approximately 80% of new HIV infections, while mother-to-child transmission contributes approximately 20%. In 2009 an estimated 120 000 new HIV infections occurred and 64 000 people died from AIDS-related illnesses (UAC, 2010, UNAIDS, 2010).

Uganda has been able to increase HIV awareness and significantly reduce adult HIV prevalence, from a peak of 18% in 1992 to 6.4% in 2007 (UAC, 2007; UAC, 2008; UAC, 2010b; Uganda Bureau of Statisitics (UBOS), 2009). According to the MOH, 379 551 PLHIV (303 088 adults, 76 463 children) are in need of ART in the country, based on a CD4 T-cell count cut-off of CD4 < 200/µl for ART initiation. The figure increases to 540 094 PLHIV (463 344 adults, 76 750 children) if the WHO-recommended ART eligibility criterion for ART initiation of CD4 < 350/µl is used. Based on the current number of active ART clients, the coverage of ART in the country is 57.5% of eligible individuals (66% adults, 24% children) based on a CD4 < 200/µl. The coverage decreases to approximately 40% of eligible individuals (43% adults, 24% children) based on a CD4 <350/µl. Overall, only a fraction of facilities in the country prescribe ART, and this is mostly at hospitals and health centres at level IV (see below) (MOH, 2010).

Delivery of health services in Uganda is under the stewardship of the MOH, which is responsible for mobilising resources and overall budgeting, policy formulation and regulation and policy dialogue with development partners. Other functions of the MOH include strategic planning, quality assurance, capacity development, technical support supervision and monitoring and evaluation of the overall sector performance. The delivery of services is provided by both the public and private sector. The private sector comprises of private not for profit organisations, private health practitioners and traditional and complementary medicine practitioners. The public sector is organised in a hierarchical order, as follows: the village level (level I), traditionally called village health teams; health centre level II, serving a parish; health centre III serving a subcounty; health centre IV serving a county (also called a health subdistrict); general hospitals serving one or more districts; regional referral hospitals, and national referral hospitals, which are self-accounting and autonomous institutions. The public sector services are based on providing a

minimum health care package which has been developed for every level of service delivery (Table 2), (MOH, 2009, MOH, 2005a).

Table 2. The Uganda National Public Health System Structure.

Health unit	Physical structure	Location	Population
Health centre I (village health teams)	None	Village	1000
Health centre II	Outpatient services (OPD)	Parish	5000
Health centre IIII	OPD, maternal, laboratory, general ward	Subcounty	10 000
Health centre IV	OPD, maternal, laboratory, general ward, theatre, blood transfusion	County	100 000
General hospital	Hospital, laboratory and X-ray	District	100 000-1 000 000
Regional referral hospital	Specialist services	3-5 districts	1-2 million
National referral hospital	Advanced tertiary care	National	>20 000 000

Adapted from the Uganda MOH Health Sector Strategic Plan 2000/01-2004/05.

1.3 The HIV epidemic response in Uganda

Since the late 1980s Uganda has adopted an open and multisectoral nationwide response to the HIV epidemic. The UAC is mandated to oversee, plan and coordinate AIDS prevention and control activities throughout the country (UAC, 2007). In collaboration with other partners, the commission has been able to complete several policies to serve its mandate. Some of these include the National AIDS Policy, the cotrimoxazole prophylaxis policy, the ART policy and guidelines for HIV counselling and testing (HCT), prevention of mother-to-child transmission (PMTCT) and orphaned and vulnerable children services (UAC, 2010). There are also other complementary policies for delivery of appropriate HIV care in the country, such as the National Health Policy I and II and the Health Sector Strategic Plans I and II, (MOH, 2009, MOH, 2005a).

The overall goal driving current HIV care activities in Uganda is to achieve universal access targets for HIV/AIDS prevention, care, treatment and social support by 2012. The goal will be attained through reducing the HIV incidence rate by 40% and improving the quality of life of PLHIV by mitigating the health effects of HIV/AIDS by 2012. Other strategies include reducing the social, cultural and economic effects of HIV/AIDS at individual, household and community

levels, and building an effective support system for quality, equitable and timely service delivery (UAC, 2010). Attaining this goal, however, calls for measures that would ensure timely and effective compliance to the domains of comprehensive HIV care and support (Hallett *et al.*, 2008; Hammer *et al*., 2008; Nakanjako *et al*., 2009).

2.0 COMPREHENSIVE HIV/AIDS CARE AND SUPPORT

Comprehensive HIV/AIDS care and support is a relatively new phenomenon in the management of HIV/AIDS. The care constitutes a systematic ladder of ascendance from HCT to pre-ARV care to ART. It is intended not only for PLHIV but also for all those directly affected by HIV (families, friends, children and those who provide care and support from the community). The service endeavours to respond to the holistic needs of PLHIV at all stages of HIV infection and attempts to slow progression and maintain the person at the highest functional level. Its component domains include provision of HCT, and clinical, psychosocial, nutritional, legal, economic, family social and community support for PLHIV. Appropriate care and support for HIV should involve the PLHIV themselves or those affected by HIV in the choice, design and delivery of the services. It should also ensure equitable access to the services, information about the services, and have respect for client autonomy (UCAID, 2008; UNAIDS *et al*., 2004; Ritzenthaler, 2005; Nakanjako *et al*., 2009; MOH, 2003a).

2.1 HIV counselling and testing (HCT)

HCT is the key entry-point to all HIV prevention, treatment, care and support services. Through HCT people discover their HIV status and its implications and make informed choices for their future life. HCT reduces the risk of acquiring or transmitting HIV through positive behavioural change. It also encourages disclosure and subsequent social support and reduces denial, stigma and discrimination. The counselling enables PLHIV to make informed decisions about family planning and promotes access to early medical care for opportunistic infections and sexually transmitted infections (STIs), (MOH, 2005b, UNAIDS, 1997). HCT can be client-initiated VCT or provider-initiated HIV counselling and testing (PIHCT).

VCT is an HIV-prevention intervention initiated by the client at his or her free will. It provides the opportunity for the client to confidentially explore and understand his/her HIV risks and to learn his/her HIV infection status with the support of a counsellor. VCT can be done in areas with no physical structure (free-standing). It may also be health unit-based or through outreach services such as home-based care. Either way, however, there must an appropriate referral system

for the client to access other components of comprehensive HIV care once they test HIV-positive (MOH, 2005b).

Provider-initiated counselling (PIHCT) is the routine testing of patients provided and initiated by a health provider. It can be diagnostic in clients who need an HIV test for medical reasons because the patient presents with symptoms that may be attributable to HIV or has an illness associated with HIV. PIHCT can also be done through routine counselling and testing. Routine counselling and testing is offered as part of the clinical evaluation of all patients in settings where HIV is prevalent. It constitutes "opt-in" where an HIV test is routinely recommended and offered to each patient and the patient explicitly consents to receive the HIV test. It may also be "opt-out" where an HIV test is routinely recommended and provided to each patient and the patient is informed of his/her right to refuse the test. In certain circumstances, such as tissue donation and medicolegal circumstances such as rape and defilement, however, HIV testing can be mandatory and may be done regardless of consent (MOH, 2005b).

Ideally, newly screened PLHIV should be enrolled for pre-ARV care. Unfortunately, most PLHIV are not aware of their HIV status. In SSA only about 12% of men and 10% of women know their HIV status (UNAIDS, 2010). In Uganda, data from a national sero-behavioural survey showed that only 15% of the adult population is aware of their HIV sero status (MOH, 2006).

Some of the identified barriers or motivators for uptake of VCT include age, high education and knowledge about HIV (Sherr *et al.*, 2007). Others are occupation, transportation difficulties, health status, ethnicity, high-risk behaviour, perceiving oneself as low risk, fear of unsolicited disclosure, fear of stigma and discrimination, male gender, having more than one sexual partner within the past 6 months, being married and using alcohol (Ma *et al.*, 2007; Rou *et al.*, 2009). Recent developments in the area of cotrimoxazole prophylaxis, tuberculosis preventive therapies and PMTCT have focused attention on expanding access to VCT as a vital component of comprehensive HIV care (Taegtmeyer, 2004, WHO/UNAIDS, 2005, RTI, 2010, UNAIDS, 2001).

2.2 Pre-Antiretroviral (Pre-ARV) care

Pre-ARV care is given to PLHIV before they are eligible for ART. It constitutes psychosocial support, nutritional care, ongoing counselling, cotrimoxazole prophylaxis to prevent opportunistic infections and routine monitoring of PLHIV to assess their eligibility for ART (MOH, 2003, MOH, 2004, Losina et al., 2010). PLHIV should access this service through quarterly visits and clinical check-ups at health facilities (Hallett et al., 2008, Losina et al., 2010). Although the global proportion of PLHIV under pre-ARV care is not comprehensively documented, UNAIDS estimates that 15% of all PLHIV have AIDS and are hence eligible for ART. By implication therefore 85% (28.3 million) of all PLHIV are supposed to be under pre-ARV care (UNAIDS, 2010). Few of them, however, enrol and adhere to the continuum of pre-ARV care, and loss to follow-up is high, especially in SSA (UNAIDS, 2009). Consequently, many PLHIV lost to follow-up do not benefit from the public health advantages this care is meant to provide.

2.3 Antiretroviral therapy (ART)

ART involves the use of at least three ARV drugs to maximally suppress HIV and stop progression of HIV disease in PLHIV. Huge reductions have been seen in rates of death and suffering when use is made of a potent ARV regimen among PLHIV (WHO, 2010). In 2009 5.2 million (36%) of the approximately 15 million people who needed ART in low- and middle-income countries worldwide received it. This in effect means 9.8 million PLHIV in need of ART in these countries could not access ART (UNAIDS, 2010).

In Uganda it is recommended to initiate ART in adults and adolescents with documented HIV infection and; CD4 cell count of 250 cells/ µl and below or CD4 cell count above 250 but below 350 cells/ µl in those who are co-infected with tuberculosis (TB), or WHO Stage III disease and women who are pregnant. Clients with WHO Stage IV disease irrespective of CD4 cell count or WHO stage I or II with CD4 cell counts are also recommended to initiate ART (MOH, 2003, WHO, 2003a, MOH, 2008). Recently, however, the WHO in a rapid advice report recommended ART initiation for PLHIV at CD4 cell counts of <350/µl (WHO, 2009a). However, because of inadequate drugs and supplies and an already over-stretched health system, the Uganda

government still uses the 2008 treatment guidelines that provide for initiation of ART at CD4 cell counts of <250/µl (Nakanjako et al., 2009, MOH, 2010).

The recent WHO guidelines from 2010 on the threshold for ART initiation (CD4< 350/µl) will increase even further the number of PLHIV requiring ART, especially in resource-poor settings (UN, 2010, WHO, 2009a). The new recommendation also raises the debate on whether PLHIV who initiate ART at a CD4 cell count of <250/µl should be labelled as timely or late ART initiators, given the difference in the national and WHO recommended threshold for ART initiation.

Table 3. WHO clinical staging for HIV infection.

Clinical Stage I:

1. Asymptomatic
2. Persistent generalised lymphadenopathy

Performance Scale 1: Asymptomatic, normal activity

Clinical Stage II:

1. Moderate weight loss (less than 10% of presumed or measured body weight)
2. Minor mucocutaneous manifestations (seborrhoeic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular stomatitis)
3. Herpes zoster within the last 5 years
4. Recurrent upper respiratory tract infections, e.g., bacterial sinusitis, tonsillitis, otitis media and pharyngitis

And/or Performance Scale 2: Symptomatic but normal activity

Clinical Stage III:

1. Severe weight loss (more than 10% of presumed or measured body weight)
2. Unexplained chronic diarrhoea for more than 1 month
3. Unexplained prolonged fever, intermittent or constant, for more than 1 month
4. Oral candidiasis
5. Oral hairy leukoplakia
6. Pulmonary tuberculosis (current)
7. Severe bacterial infections such as pneumonias, pyomyositis, empyema, bacteremia or meningitis
8. Acute necrotizing ulcerstive stomatitis, gingivitis or periodontitis
9. Unexplained anemia (<8gm/dl), neutropenia (<0.5× 10^9 per litre), or chronic thrombocytopenia (<50× 10^9 per litre)

And/or Performance Scale 3: Bed-ridden for less than 50% of the day during the last month

Clinical Stage IV:

1. HIV wasting syndrome – weight loss of more than 10%, and either unexplained chronic diarrhoea for more than 1 month, or chronic weakness or unexplained prolonged fever for more than 1 month
2. *Pneumocystis pneumonia* (PCP)
3. Recurrent severe bacterial pneumonia
4. *Toxoplasmosis of the brain*
5. Cryptosporidiosis with diarrhoea for more than 1 month
6. Chronic isosporiasis
7. Extrapulmonary cryptococcosis including meningitis
8. Cytomegalovirus infection (retinitis or infection of other organs)
9. Herpes simplex virus (HSV) infection, mucocutaneous for more than 1 month, or visceral at any site
10. Progressive multifocal leukoencephalopathy (PML)
11. Any disseminated endemic mycosis such as histoplasmosis, coccidioidomycosis
12. Candidiasis of the oesophagus, trachea, bronchi or lungs
13. Atypical mycobacteriosis, disseminated
14. Recurrent non-typhoid salmonella septicaemia
15. Extrapulmonary tuberculosis
16. Lymphoma
17. Invasive cancer of the cervix
18. Kaposi's sarcoma
19. HIV encephalopathy – disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing slowly over weeks or months, in the absence of concurrent illness or condition other than HIV infection that could account for the findings
20. Atypical disseminated leishmaniasis
21. Symptomatic HIV-associated nephropathy or symptomatic HIV associated cardiomyopathy

And/or Performance Scale 4: Bed-ridden for more than 50% of the day during the last month

Source WHO 2008

2.4 Health system components and functions

The WHO defines a health system as all the activities whose primary purpose is to promote, restore or maintain the health of the people. The six building blocks of a health system include service delivery, human resources for health, health care financing, drugs and supplies, health management information systems and leadership and governance (WHO, 2011b). A good health system should be able to deliver quality services to all people when and where they need them, although the specific configuration of services may vary from country to country. Such a system would require adequate health care financing, well-trained and adequately paid workers and a reliable information management system for decision-making and policy formulation and regulation. In addition, good leadership and governance, well maintained facilities, equipment, drugs and supplies and logistics are needed to deliver quality health care (WHO, 2011b).

2.4.1 Health system challenges in Uganda

Like many resource-poor settings, Uganda faces multiple challenges in her endeavour to deliver health services including comprehensive HIV care to the population. The main challenges of the Uganda health system are scarcity of human resources for health, lack of infrastructure and equipment, poor health care financing and inadequate drugs and supplies to meet client demands.

Human resources for health

Trained and skilled staff are vital in delivering comprehensive health care. However, in Uganda human resources for health are too scarce to meet the service demands, leading to a heavy workload on those who are available. A report by the Uganda MOH indicates that by November 2008, only 51% of approved positions had been filled at national level. The scarcity of health personnel is more critical in conflict, post-conflict, rural and hard to reach areas.

This sector in Uganda is also characterised by insufficient training capacity for health workers with the right mixture of skills to meet the needs of the people, low remuneration and poor working conditions. In addition, health workers are inequitably distributed, with many preferring to work in urban areas. Many health workers have also migrated to other countries in search of attractive salaries and opportunities. Absenteeism, dualism and the poor attitude of health workers towards patients is a common reality in many government units (MOH, 2009, UAC, 2010).

Health infrastructure

In Uganda the current population living within 5 km of a health facility, including both public and private units, is 72% (MOH, 2009). However, many government facilities lack appropriate equipment and are in a state of disrepair. The hospitals are congested with few beds, and in such facilities floor cases are numerous. There has been little rehabilitation of buildings and maintenance of medical equipment at all levels of service delivery. Most facilities in the rural and hard to reach areas lack accommodation for staff making it hard to attract the desired personnel. The functionality of the health system with regard to infrastructure in Uganda is therefore a challenge, and systems strengthening will be required - especially at district level - to effectively deliver comprehensive HIV care among others (MOH, 2009).

Table 4. Coverage of ART services by level of facility in Uganda, September 2009.

Health facility level	Total No. of facilities	No. of facilities providing ART	%
National referral hospitals	2	2	100
Regional referral hospitals	11	11	100
General hospitals	98	98	100
Health centre IV	166	130	78
Health centre III	905	40	4
Health centre II	1887	2	0.1
Research programmes	N/A	4	
Specialised clinics	N/A	31	
Private for profit clinics	Unknown	52	
Total		374	

N/A = not applicable. Source: MOH, 2009.

Drugs and supplies

A good health care system should be able to deliver adequate quantities of affordable, good-quality essential drugs and supplies to all those who need them (WHO, 2011a). In Uganda approximately 70% of government health units have monthly stock-outs of any indicator medicine. In addition, only 30% of the essential medical health supplies are provided for in the national budget (MOH, 2009). Global initiatives remain the basic providers of resources needed for malaria, HIV/AIDS, TB, vaccines and reproductive health commodities. During the financial year 2006/7, for example, the contribution from global initiatives was US $2.39 per capita out of the total US $4.00 per capita spent on the above services (MOH, 2009). Clients who can afford to do so therefore resort to the private sector for essential medical and health supplies, in spite of the high costs. About 90% of all medicines are imported. Counterfeit drugs are also becoming an increasing problem in Uganda, especially in the private for profit sector (MOH, 2009).

The MOH attributes stock-outs to extensive institutional arrangements, overload of the national medical stores, inadequate financing and delayed and incomplete reporting, which makes quantification of the desired drugs and supplies difficult (UAC, 2010, MOH, 2010).

Funding for health care

Uganda's health expenditure as a proportion of the government's discretionary expenditure has remained relatively stable at 9.6%, still below the Abuja Declaration target of 15% (MOH, 2009, UBOS, 2009). Although the private sector charges user fees, there is no user fee for public lower-level health units and general wings of publicly owned hospitals. Health insurance is a preserve of the lucky few and is subsidised by employers on behalf of their employees (MOH, 2009).

Most costs for health care in Uganda (50%) are incurred by households out of pocket, followed by donors (35%) and then Government (15%). Financing has been largely inadequate to enable provision of the Uganda National Minimum Health Care Package at almost all levels of service delivery. For example, while the MOH anticipated per capita costs for 2011/2012 to be US $47.9, the Medium-term Expenditure Framework for the same period is estimated at US $12.5 - a shortfall of almost US $29 (MOH, 2009). A recent study in Uganda showed that while recurrent expenditure on primary health care had increased by almost 70 times in the last 10 years, key aspects that would facilitate its realisation were not addressed (Mugisha and Nabyonga-Orem, 2010). There is a need therefore for an optimal balance in investment in the different inputs to ensure efficiency in health spending. In view of the low health expenditure per capita, inadequate human resources, inadequate drugs and supplies and limited health infrastructure, there is a need to adopt community-oriented access approaches that will deliver comprehensive HIV care to those who need it.

2.5 Uptake of pre-antiretroviral care

Research has been done on barriers to uptake of ART in resource-poor settings. Identified barriers to uptake of ART in such settings include cost, food insufficiency, distance to clinic, women's lack of decision-making power, stigma, poverty, fear of medication, lack of information and belief in traditional medicine (Mshana et al., 2006, Wilson and Blower, 2007, Muula et al., 2007, Unge et al., 2008, Plummer et al., 2006). However, little is known about barriers to uptake of pre-ARV care, and the socio-contextual and policy issues for pre-ARV care may be different from those for ART. Pre-ARV clients are, for example, likely to be physically strong and going about

their work normally compared to ART-eligible clients. They may not therefore perceive themselves as being susceptible to any danger if they do not take up pre-ARV care, contrary to ART-eligible clients who are likely to be sick enough to warrant health care-seeking.

2.5.1 Loss to follow-up of PLHIV under pre-ARV

Retention of PLHIV under comprehensive HIV care is a vital strategy for the overall management of PLHIV (UNAIDS, 2010). Unfortunately, many PLHIV are lost to follow-up during HIV care, especially during pre-ARV care in SSA (Long, 2008, Losina et al., 2010, Larson et al., 2010). In Uganda, maintenance of care and retention of clients under comprehensive HIV care is still minimal since follow-up is still very low, except where there are network support agents for PLHIV (MOH, 2010). The network support agents have remained active, especially in places where civil society organisations have strong partnerships with the health facilities to provide both counselling and general HIV/AIDS care at facility level, and in the communities (MOH, 2010, UAC, 2010).

A lot of research has been done on barriers to retention and adherence to ART in both high and low income settings (Ezzy et al., 1998, Hardon et al., 2007, Unge et al., 2010, Nakanjako et al., 2009, Alice Nakiyemba et al., 2004). Some of the barriers identified by these studies include young age, low education status, financial constraints, weak health care infrastructure, few and poorly trained health staff, pervasive stigma, lack of social support, lack of harm reduction protocols and poor supply of drugs. Others include co-morbidities, fatigue, hunger, waiting time and transport costs, drug side-effects, failure to carry drugs on travel, poverty, beliefs, fear of side-effects, religious practices and negative attitudes from religious leaders. However, little is known about reasons for loss to follow-up of PLHIV under pre-ARV, especially in the context of Uganda where HIV and ART awareness are presumed to be high.

2.5.2 Delayed initiation of antiretroviral therapy

Delayed initiation of ART for PLHIV is a major concern, especially at a time when WHO is advocating for earlier ART initiation at a CD4 cell count of <350 cells/µl (Hammer et al., 2008, Sterne et al., 2009, WHO, 2009a). Delayed initiation of ART is associated with late-stage diagnosis and results in high rates of HIV-related morbidity and mortality (WHO, 2009b). In

SSA, while the overall coverage of ART initiation has increased to 37% of those in need, emerging evidence shows that up to 59% of PLHIV in SSA are either lost to follow-up or start ART at a very late stage of the disease (UNAIDS, 2010, Tsague, 2008).

Recent studies also show that 40% of PLHIV in Uganda present for HIV care late or very late, at WHO disease stages III or IV, many with CD4 cell counts of <50 cells/µl (Smart, 2007, Kigozi et al., 2009, Battegay et al., 2008). The Ugandan HIV/AIDS National Strategic Plan 2007/8 – 2011/12 projected an increase in ART coverage to about 80% by 2011/12. However, limited uptake of and delayed access to HIV services are still a major stumbling block to reaching these targets (UAC, 2007). There is a paucity of information on why PLHIV would initiate ART very late in a country where HIV and ART awareness are presumably high (UAC, 2007).

2.6 Role of low-cost interventions in comprehensive HIV care

Because of poverty and a limited health infrastructure for increasing access to the rural poor and most vulnerable, many multilateral organisations and health programmes such as UNICEF/WHO have advocated for an integrated community case approach for fevers in children in order to reach the poor (Bryce et al., 2008, WHO/UNICEF, 2004). Programmes such as the integrated community case management for malaria and the home-based management of fever have produced increased access to treatment for malaria and/or pneumonia (Winch *et al*., 2005, Nsungwa-Sabiiti *et al*., 2007, Haines *et al.*, 2007).

Smilarly, home-based care programmes for HIV/ART piloted in many resource-poor settings have also shown increased uptake, high retention rates for HIV care and increased adherence to ART (Weidle Paul J et al., 2006). The use of peripheral units and trained, supervised lay workers to provide ART services in Uganda has, for example, made the services more affordable, accessible, and attractive to PLHIV (Jaffar, 2009, Jaffar et al., 2005, Maskew et al., 2007). Although these pilot studies have been conducted in highly funded environments, their success gives the impetus to a trial of low-cost interventions tailored to optimal use of the available resources, as long as they increase access to comprehensive HIV care. Community health workers

or network support agents for HIV care, for example, provide a pool of trainable and supervised volunteers for increasing access to comprehensive HIV care (MOH, 2010, UAC, 2007).

3.0 THEORETICAL FRAMEWORK FOR COMPREHENSIVE HIV CARE

HIV/AIDS is a condition characterised by stigma, self-denial, discrimination and a great need for family and community social support. Furthermore, the condition requires behavioural change for the PLHIV to access prevention, care and support services. To adhere to the continuum of comprehensive HIV care, PLHIV require physical, spiritual, moral, logistical, financial and material support from their intimate partners, immediate family, close relatives, employers and other social networks to enable them overcome barriers or challenges to seeking or accessing appropriate care. In addition, there must be enabling policies and guidelines to address the socio-contextual aspects of HIV care and support to positively influence the desired behaviour change (UAC, 2007, URCS., 2008, Population-Council., 2010, Avert, 2010, IFRCRCS, 2010, UNAIDS, 2001, Feucht et al., 2007, Birbeck et al., 2009, Lieber et al., 2006).

Research has shown that individuals' choices are influenced by many factors acting at different levels, ranging from the intrapersonal and interpersonal to the community and society in general (Fleury and Lee, 2006, Facoine P and Facoine N, 2007). Any successful intervention in care and support for PLHIV must therefore take into consideration the interrelated levels of influence which go beyond the individual PLHIV, but also the health care delivery system and their environment (DiClemente et al., 2004, DiClemente et al., 2005, Campbell et al., 2007, Sallis JF and Owen N, 2002, CARE, 2010). All these concepts, which are vital to this thesis, are well defined by the socio ecological model (SEM), which we used to define and discuss client and system determinants for pre-ARV care and ART initiation.

3.1 The socio ecological model

The socio-ecological model (SEM) is based on the intertwined relationship between the individual and the environment (Sallis JF and Owen N, 2002, Moore, 2001). The model caters for the multiple levels of influence for behaviour change and actions including intrapersonal (biological, psychological), interpersonal (social, cultural, attitudinal), organisational, community, physical environmental and policy outlines or guidelines. It therefore offers an explicit direction guiding the development of more comprehensive population-wide interventions. The model also recognises that behaviour change is expected to be maximised when environments and policies

support healthful choices, when social norms and social support for healthful choices are strong and when individuals are motivated and educated to make those choices (McMurray, 2006). More importantly, the model can be used to develop comprehensive intervention approaches that systematically target mechanisms of change at each level of influence (Stokols et al., 1996, Fleury and Lee, 2006, McLeroy et al., 1988, Moore, 2001).

This thesis uses the SEM to explore reasons for loss to follow-up of PLHIV from pre-ARV care (paper I) and very late initiation of ART (paper III) with regard to the policy, the views of PLHIV, their families, social networks and the community in which they live. The thesis also evaluates the effect of modified policy guidelines complemented by a community component on uptake of pre-ARV care (paper II), and assesses crucial risk factors for very late initiation of ART (paper IV), based on individual, community and policy-guided variables.

Figure 1. A multiple-level schematic drawing of the SEM (Modified from Sallis and Owen, 2002).

4.0 RATIONALE FOR THE STUDIES

Uganda has been heralded as a success story in the fight against AIDS, having adopted an early, open and multisectoral national response to the HIV epidemic. This response has increased HIV awareness and contributed to the significant reductions seen in adult HIV prevalence, from a peak of 18% in 1992 to 6.4% in 2007. However, reports about Uganda indicate that in spite of these achievements, a large proportion of PLHIV (90%) in some districts either do not take up or are lost to follow-up during pre-ARV care, and consequently many PLHIV initiate ART very late (at a CD4 count below 50 cells/µl), with a much higher risk of early mortality (Lutalo et al., 2009, Smart, 2007, Kigozi et al., 2009, DHO, 2009). Failure to take up or loss to follow up of PLHIV during pre-ARV care and very late ART initiation are major barriers to scaling up access to ART in Uganda, especially when global efforts are being driven towards earlier ART initiation, already at a CD4 count of < 350 cells/µl (Hammer et al., 2008, WHO, 2009a).

There is little information on reasons for failure to take up or loss to follow-up of PLHIV during pre-ARV care and barriers to or motivators for very late initiation of ART in the context of Uganda, where HIV and ART awareness are presumably high. Available literature captures determinants for uptake of VCT, ART and non-adherence to ART in low- and high-income countries (Kumarasamy et al., 2005, Knodel et al., 2010, Chesney et al., 2000, Bangsberg et al., 2000, Byakika-Tusiime et al., 2005). Generalising this literature to pre-ARV care is, however, exigent since the challenges, barriers or practical policy implications for uptake and loss to follow-up during pre-ARV may be different because the health situation, care demands and social-psychological contexts for PLHIV without AIDS and those with AIDS are different. There is also a lack of literature on feasible, community-oriented, low-cost interventions likely to improve uptake of pre-ARV care and subsequent timely initiation of ART in resource-poor settings.

The purpose of this thesis is to explore reasons for failure to take up or loss to follow-up of PLHIV during pre-ARV care from the perspective of the PLHIV themselves, in order to evaluate low-cost interventions for enhancing regular pre-ARV care and subsequent timely initiation of

ART in Uganda. The thesis also seeks to understand and assess crucial risk factors for very late initiation of ART in Uganda for purposes of policy advocacy and planning.

We therefore explore the views of PLHIV who did not take up or had been lost to follow-up during pre-ARV care and their caretakers on reasons for non-uptake or loss to follow-up during pre-ARV care, and evaluate the effect of low-cost interventions on uptake of pre-ARV care. We also seek the views of PLHIV who had initiated ART in time and those who initiated ART very late and their caretakers on reasons for very late initiation of ART, and assess crucial risk factors for very late initiation of ART in eastern Uganda.

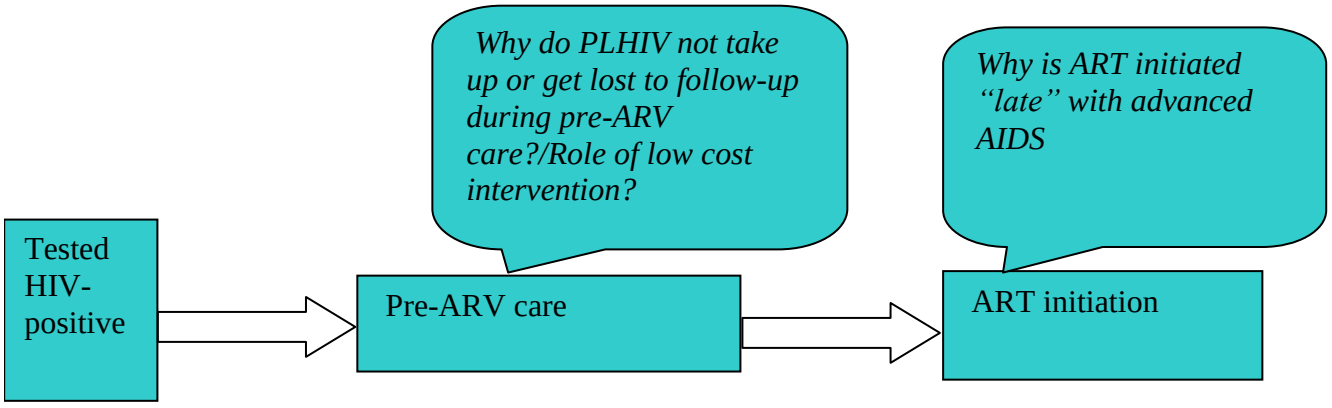

Figure 2. Schematic framework for HIV/AIDS care and research questions analysed in this thesis

5.0 AIM AND OBJECTIVES

5.1 Aim

To investigate uptake and loss to follow-up of people living with HIV under pre-ARV care and delayed initiation of ART among PLHIV in Iganga district, Uganda, in order to inform policy and strategic planning for improving comprehensive HIV/AIDS care.

5.2 Objectives

I. To explore reasons for loss to follow-up of PLHIV under pre-ARV care from the perspective of the staff and PLHIV in Iganga district, Uganda (sub-study I)

II. To evaluate the effect of extended counselling on uptake of pre-ARV care in Iganga district, Uganda (sub-study II).

III. To understand reasons for delayed ART initiation from the PLHIV/caretakers' own perspectives in Iganga district, Uganda (sub-study III).

IV. To assess risk factors for very late initiation of ART in Iganga district, Uganda (sub-study IV).

6.0 METHODS

6.1 Study area and study population

The studies in this thesis were conducted in Iganga district located in the east of the republic of Uganda. Uganda is a landlocked country located in East Africa covering an area of 241 550.7 km^2, of which 41743 km^2 are open water and swamps, and 199 807 km^2 is land. The projected total population by 2010 is 30.7 million people with a median age of 15 years (UBOS, 2009). Iganga district is one of the 112 administrative districts that constitute the country, with an approximate population of 600 000 people. The district is located 115 km east of the capital, Kampala (Figure 3). The area is predominantly rural with only about 7% living in an urban or peri-urban environment. The majority of the people belong to the Bantu ethnic tribe called Basoga, most of whom depend on subsistence farming of food crops.

There are 101 health units in the district, 83 of which are owned by the Government and 18 by NGOs. District ART services are organised according to the Uganda national hierarchical referral system, where 70 of the units are health centres; 2 (HC II) offering only cotrimoxazole refills and home-based care services to PLHIV; 27 are HC III offering VCT, pre-ARV and home-based care services to PLHIV; and 3 HC IV and 1 general hospital offer routine counselling and testing, home-based care, pre-ARV care and ART services to PLHIV. Other care providers include over 200 private drugstores/private clinics located in Iganga town and several other smaller towns scattered around the district. Most of the drugs commonly found in these drugstores and clinics include painkillers, assorted antibiotics and cheap antimalarials, but no ARVs. There are no other accredited ART providers in the district, although over 100 traditional and spiritual healers are presumed by the community to offer “similar” services (DHO, 2009).

Prospective and current ARV users, health workers and managers as well as members of the community in the district were interviewed for this thesis.

Figure 3. Map of Uganda showing the study district (Iganga).

Over 30 000 people (5.3% of the district's adult population) currently live with HIV in Iganga district and 4500 PLHIV are presumed to be eligible for ART according to the national threshold for ART initiation of CD4 <200 cells/µl (MOH, 2006, UNAIDS/WHO, 2007). Currently only 1150 PLHIV (i.e. approximately 25% of those in need) are known to access ART in the district

Approximately, 40% (360 out of 900) of PLHIV who initiated ART between 2004 and 2009 at Iganga hospital had a CD4 count of <50 cells/µl, with a median of 126 (range 14-198 cells/µl). Similarly, only 10% of the clients who tested HIV-positive for the first time between 2004 and 2007 at the hospital took up and regularly attended pre-ARV services, while 90% have been lost to follow-up.

Until 2008, when two more health centres were accredited to offer ART services, ART could only be accessed at Iganga General Hospital. The Iganga district ART services, occasionally managed by a medical doctor but more often by an assistant physician or a nurse and offering refills of ARVs and cotrimoxazole, adherence counselling, and psychosocial and nutritional support once a week, are quite representative of HIV care in rural Uganda (DHO, 2008).

6.2 Study design

We employed both qualitative and quantitative methods for the studies in this thesis. Qualitative methods were used to get an in-depth understanding of the awareness, experiences, views, beliefs, sociocultural and contextual factors that influenced PLHIV behaviour towards regular pre-ARV care and timely/late initiation of ART. We thus conducted key informant interviews (KIIs) with staff at the pre-ARV clinic, focus group discussions (FGDs) with caretakers of PLHIV and in-depth interviews (IDIs) with PLHIV, half of whom had dropped out of pre-ARV care, for study I. We also conducted IDIs with PLHIV who initiated ART at 50 - 200 CD4 cells/µl and those who initiated very late, at CD4 < 50 cells/µl, and FGDs with caretakers of PLHIV on ART to get an in-depth understanding of reasons for delayed initiation of ART for study III.

One quantitative design used was a randomised controlled trial whose participants were newly screened PLHIV to evaluate the effect of extended counselling on uptake of pre-ARV care, in study II. The other was an unmatched case-control study where PLHIV who started ART with a

CD4 cell count of <50 cells/µl (very late initiators) were classified as cases and PLHIV who initiated ART at CD4 between 50-200 cells/µl (late initiators) were the controls. The objective was to assess risk factors for very late initiation of ART in study IV.

6.3 Data collection methods

6.3.1 Qualitative methods

Qualitative research is an inquiry process of understanding based on distinct methodological traditions of inquiry that explore a social or human problem. The researcher builds a complex, holistic picture, analyses words, reports detailed interviews with informants and conducts the study in a natural setting. It is therefore important that the researcher or research team understand the sociocontextual aspects of the subject under study (Dahlgren *et al.*, 2004). The research team for the qualitative studies was multi-disciplinary, and included an indigenous public health physician who has managed PLHIV in the area for over 10 years and a social scientist with experience in conducting similar research in the study setting. Other members were research assistants who moderated and took notes for the study. They were from the district and spoke and understood the native language. The inquiry methods employed included FGDs, KIIs and IDIs.

Focus group discussions (FGDs)

An FGD enables the researcher to get an understanding from a group of people about their perceptions, opinions, beliefs, values, understanding and attitudes towards a product, service, concept or other ideas. Questions are asked in an interactive group setting where participants are free to talk with each other (Henderson and Naomi R, 2009, Kitzinger, 2005). Participants in FGDs are specifically selected to explore the range of beliefs in a study population. The group dynamics in an FGD facilitate the collection of relatively detailed information on prevalent attitudes, ideas, conflicts and contradictions. The interaction among the participants in FDGs is useful in exploring the individuals' contextual views about the subject of study. FGDs therefore generate more information about a subject, because participants are able to build on each others' response (Dahlgren et al., 2004, Khan and Manderson, 1992, Rice P L and Ezzy, 1999, Holloway, 2008). Because they are subjective, FGDs allow the researcher to access different types of communication such as laughter, teasing, jokes, anecdotes or arguments, which may reveal more than what people ordinarily share (Stewart DW et al., 2007). The disadvantages of FGDs are that

sometimes minority opinions are suppressed, and if not carefully conducted the researcher is likely to drive the group interaction on his own perceptions about the topic of study. Also, because of group dynamics FGDs may not generate the individual complex beliefs and practices within the group (Rice P L and Ezzy, 1999, Hardon A et al., 2001).

In study I we conducted FGDs with friends or relatives who lived with or cared for PLHIV to explore their attitudes and awareness about pre-ARV care. The FGD participants were volunteered by the respective PLHIV. Attitudes towards pre-ARV care among these informants influence the health care-seeking decisions made by PLHIV. In all six FGDs were conducted, three with men and three with women. Each FGD had 6 - 12 participants, constituting 59 participants in total. The FGD guide explored knowledge on pre-ARV care and its importance, perceptions about pre-ARV services and knowledge about availability and packages of services and challenges/barriers to access to pre-ARV services.

In study III FGDs were conducted with community members who lived with or looked after the ART clients to generate debate and explore views on reasons for late ART initiation. The FGD participants were volunteered by the respective ART clients. In total 10 FGDs were conducted, five with men and five with women, separately, to give participants a chance to express themselves more freely. Each group comprised 6 - 12 participants, reaching a total of 112 members. FGDs were not carried out with the PLHIV because many of them had not disclosed their status to outsiders, and they therefore did not want to discuss their personal treatment in groups.

Key informant interviews (KIIs)

KIIs are used in qualitative research to explore the subjective meanings and interpretations which individuals give to their experiences. KIIs are a way to obtain information from people who are in a position to know not only what individuals or the community do but why they do it. Key informants are normally chosen on the basis that they have special assets that make them knowledgeable about the topic of interest (Marshall and Rossman, 2006).

In study I five KIIs were held to understand the views of the health managers and providers on client or system barriers or facilitators for uptake and loss to follow-up of PLHIV under pre-ARV care. They were chosen on the basis of their experience in managing PLHIV. The KII participants were purposively selected from Government facilities since no non-governmental clinics offered comprehensive HIV care in the district during the period under study. All the KIIs with the managers or providers were conducted in English.

Indepth interviews (IDIs)

An IDI is a qualitative research method which proceeds as a confidential and secure conversation between an interviewer and a respondent. The method allows the researcher to get the inside views, opinions, beliefs or other social contextual issues related to the topic of study in the respondents' own environment. The method can thus produce exhaustive and varied knowledge from the interviewee experiences, opinions, beliefs or motives, which group interviews would not elicit. It is a suitable method if the subject of research is very sensitive or controversial. IDIs give the respondent time in peace to develop and give reasons or perceived meanings without being influenced by the opinions of others (Megafon, 2000, WHO, 2004, Lisa A and Guion, 2000, Holloway, 2008, Gretchen R Webber et al., 2010).

In study I we conducted 10 IDIs, five with the PLHIV who had dropped out and five with those who regularly attended pre-ARV care from 2004 to 2007. PLHIV were selected because they were considered most knowledgeable about their own situation with regard to pre-ARV care (Boyden and Ennew, 1997). By interviewing them in their own environment, we were able to get their in-depth understanding of issues related to uptake or loss to follow-up of PLHIV under pre-ARV care. A topic guide covering individual and family background, social networks and how they influence individual decisions on health, knowledge of pre-ARV care and its perceived importance, post-VCT access to information, challenges to regular pre-ARV attendance and individual and community perceptions on pre-ARV care was used. The PLHIV who had been lost to follow up were purposively selected and traced by the staff who attended to them during VCT.

In study III we conducted a total of 20 IDIs, 10 with clients who started ART with a CD4 cell count of 50 - 200 cells/µl and 10 with clients who started ART very late (with a CD4 <50 cells/

µl). These clients were chosen because they were presumed to be more "knowledge rich" on the study topic in their own situations than anybody else. The respondents were randomly selected by their dates of starting ART using the ART registers. The two groups were chosen in order to allow comparative analysis of the factors affecting timely and late ART initiation. A guide covering individual and family background, prior pre-ARV exposure, knowledge of ART and its importance, knowledge of AIDS-defining symptoms, conditions associated with timely or late initiation of ART and social networks and how these affected individual health-seeking behaviour was used for the interviews. Interviews stopped when it was judged that a point of saturation had been reached and no more new information could be retrieved.

6.3.2 Quantitative methods

Quantitative methods are research techniques used to gather information dealing with numbers and other aspects of research that are measurable. They are used to test a hypothesis or determine an association between explanatory (independent) and outcome (dependent) variables. Statistics, charts, tables and graphs are often used to present the results of these methods. In this study we used a randomised controlled trial (RCT) and case-control design, as explained below.

Randomized controlled trial (RCT)

An RCT is one of the most powerful tools of research - a study in which people are allocated at random to receive one of several interventions. The term "intervention" refers in a wider sense to any maneuver offered to study participants that is likely to have an effect on their health status or the outcome of interest. Examples of such maneuvers are prevention strategies, screening programmes or community intervention trials. Someone who takes part in an RCT is called a participant or subject (Stolberg *et al*., 2004). Random allocation of participants is aimed at ensuring that all have the same chance of being assigned to each of the study groups (Altman, 1991). The allocation should therefore not be done by the investigators, the clinicians, or the study participants (Jadad, 1998). If randomisation is properly done, the baseline characteristics of the participants are likely to be similar across all groups (Jadad, 1998). Because of randomisation selection bias is minimised, hence balancing both known and unknown prognostic factors in the assignment of treatments. In summary, RCTs are quantitative, comparative, controlled

experiments in which investigators study two or more interventions in a series of individuals who receive them in random order (MedicineNET, 2010).

In study II we conducted an RCT with an intervention based on key messages from study I (reasons why newly screened PLHIV were not taking up or were getting lost to follow-up under pre-ARV care). The key message from study I was that the newly screened PLHIV were not getting enough post-test counselling on why and when to come back for pre-ARV care by overloaded staff. An intervention consisting of post-test counselling by staff trained in basic counselling skills, combined with monthly home visits by community support agents for ongoing counselling to newly screened PLHIV, was thus conducted in Iganga district, Uganda between July 2009 and June 2010. Participants (N=400) from three public recruitment centres were randomised to receive either the intervention, or the standard care (the existing post-test counselling, the control arm).

The design was a parallel group balanced (1:1) client randomised and single-blind superiority controlled trial. Eligible participants consisted of all newly screened HIV-infected adult clients (>18 years) at the three recruitment centres at the start of the study, who were of sound mental status and not on the prevention of mother-to-child transmission (PMTCT) programme or bound to leave the district during the period of follow-up.

The design involved following up newly screened PLHIV after post-test counselling for uptake of pre-ARV care at any health centre (level II-V) within the district, whichever was nearest to their homes, as would be jointly agreed by the counselling staff at the recruitment centre and the participant. Thus, following a positive HIV test at the RCT clinic in the three recruitment centres, participants were randomised into one of two arms: the control arm and the intervention arm. The participants in the control arm received standard care, including assignment of an identification number, declaration of the results, provision of cotrimoxazole prophylaxis and advice to the client to go for pre-ARV care at the nearest health centre every three months.

Participants in the intervention arm received another form of specialised counselling and follow-up. The specialised counselling was conducted by six health workers who had been trained in

basic counselling skills for three days at a direct financial cost of US $20 per staff member. During the training it was emphasised that those who had been trained should not share their new skills with the staff selected for the control arm. The counselling offered in the intervention arm similarly involved allocation of an identification number, declaration of the results to the client and cotrimoxazole prophylaxis. In addition, the counsellor encouraged self-disclosure of HIV status to the participant's immediate family, promoted positive living with HIV and HIV prevention and emphasised the importance of going for pre-ARV care at the nearest health centre every three months. As part of the intervention these participants were also attached to an HIV/AIDS community support agent close to their area of residence, who visited them monthly at their homes for a two-hour counselling session and reminded them to go to the nearest health centre for quarterly pre-ARV care.

HIV/AIDS community support agents are influential volunteers in the community or ART expert clients who have been sensitised and assigned the role of counselling and encouraging PLHIV to seek care and subsequently linking them to the service providers. The community support agents had been trained and registered by the district in the previous years but also received a one-day orientation about the study.

The outcome measure was the proportion of newly detected and counselled PLHIV in either arm who had been to their nearest health centre for clinical check-up in the subsequent three months after enrolment. An allowance of an extra two months to return for check-up was considered for every participant to cater for any inevitable circumstances that might prohibit the participant from going for check-up. The participants in both arms were followed up and considered to have taken up (accepted) or not taken up (not accepted) pre-ARV care according to the following definition: those who went for clinical check-up at the nearest health centre at least once in the subsequent three months (+ two months, see above) were considered to have taken up pre-ARV care, while those who missed their scheduled appointment at the pre-ARV clinic in the subsequent three months (+ two months) were considered not to have taken up pre-ARV care (Figure 4).

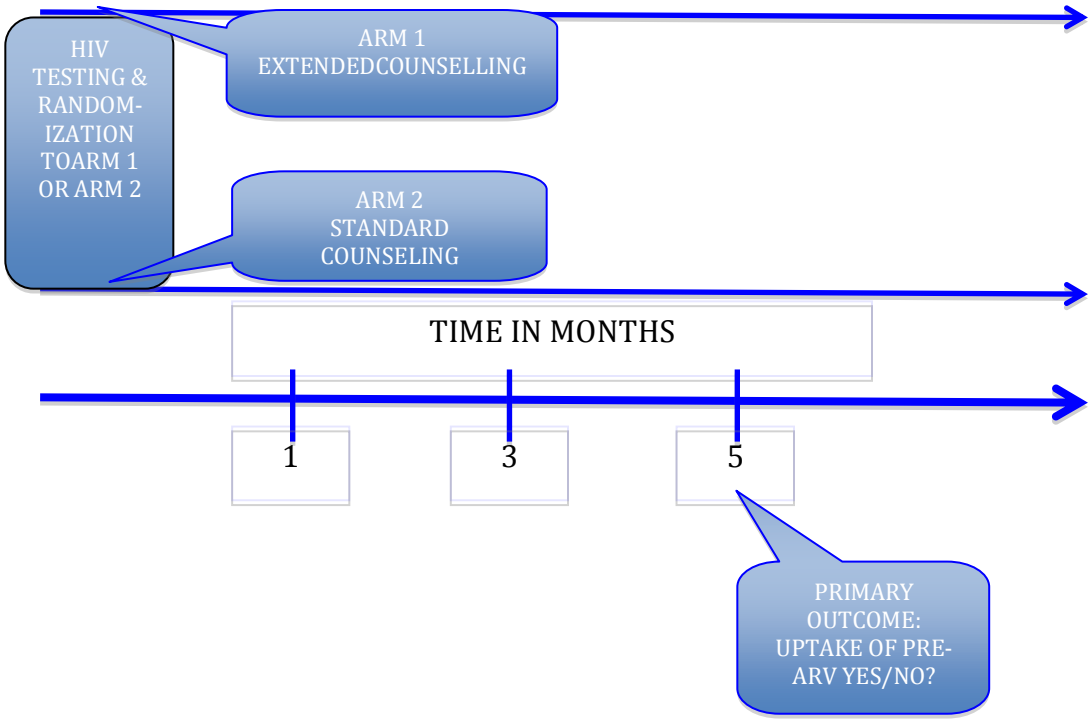

Figure 4. Description of the trial time line for assessing uptake of pre-ARV care in Iganga district.

Baseline data for every enrolled participant were collected through face-to-face interviews following a short structured questionnaire administered by a trained research assistant at each of the three recruitment centres. The baseline information included socio-demographic characteristics such as age, sex, education, religion, marital status, marriage status, occupation and number of people in the household. Information was also collected on knowledge of HIV transmission, prevention, pre-ARV care and its importance and stigma. For participants who went to their nearest health centre for pre-ARV care after three months (+ two months), information on reasons for going for care, disclosure and motivational factors for disclosure, any side-effects of cotrimoxazole, constraints to pre-ARV care seeking, condom use and number of sexual partners was also collected. The follow-up data were collected by a research assistant who had been identified at each of the participants' agreed nearest health centres.

All the counsellors and corresponding research assistants were trained for three days on the study aim, design and tools. The study tools were pre-tested using a pilot study at another health centre IV offering ART in the area. Experiences from the pilot study were discussed at an extra session

separately for each arm. Necessary changes were then made to the tools and the research assistants were given additional guidance. Throughout the study period random validity checks were conducted at the health centres by the first and second authors (LM and TN) to ensure compliance, and also to collect the completed corresponding questionnaires. The completed questionnaires were then checked for consistency, range of values and completeness.

The sample size for the RCT was calculated using a formula suggested by Bland 2000, (Altiman and Brand, 1995). At a power of 80%, with estimated pre-ARV uptake of 50% for the control arm, and a target to detect a difference of absolute 14% in the intervention arm as significant at 5% level, a minimum of 193 participants (rounded up to 200) per arm was found adequate. The number of newly screened PLHIV normally differs between the different study centres; it is twice as high at Iganga Hospital compared to Busesa and Kiyunga. Based on these proportions, 50% (200 participants, 100 in each arm) were enrolled at Iganga Hospital and 25% (100 participants, 50 in each arm) were recruited at each of the other two recruitment centres (DHO, 2009).

In all the study centres participants were randomly assigned to receive the standard post-test counselling or extended counselling. Treatment assignment was randomly generated in blocks of four, based on computer-generated random number sequences provided by one of the statisticians in the study team (DK), who had no contact with the study participants. Assignment sequences were placed in opaque sealed envelopes and appropriate numbers sent to each of the study centres.

At each centre participant enrolment was done by an assigned laboratory technician who carried out the HIV testing. After a client had tested HIV-positive, the technician at each centre asked the eligible client to pick and open an envelope from a batch of four for assignment to the appropriate arm. At each centre this procedure continued until the required allocated numbers per arm had been realised. Given the nature of the intervention, it was hard to mask the staff in the different arms as to which arm they themselves belonged to. However, none of the study subjects was informed of the details of the arm to which they had been assigned.

To limit contamination between and among the research assistants and the participants, each arm at every centre was put in different rooms at least 50 m apart. The staff members were also instructed not to share the nature and content of counselling they offered to the participants.

Case control studies

A case-control study is an analytical epidemiological study which compares individuals who have a specific disease or condition (cases) with a group of individuals without the disease or condition (controls). The proportion of each group having a history of a particular exposure or characteristic of interest is then compared. An association between the hypothesised exposure and the disease being studied will be reflected in a greater proportion of the cases being exposed. It is advantageous for the controls to come from the same population as the cases, to reduce the chance that some other difference between the groups accounts for the difference in the exposure that is under investigation (EHIB, 2008).

Case-control studies start with the outcome and look backward for the exposure. Case-control studies can be used to study infrequent (rare) diseases, and are relatively inexpensive because no follow-up is necessary. Because exposure is ascertained retrospectively, the investigator does not have to wait for the accumulation of enough individuals who are developing the disease. Some of the disadvantages of using a case-control design are that they cannot be used to compute incidence rates and they are prone to selection and recall bias (Kaelin, 2004).

In study IV we conducted an unmatched case-control study of clients initiated on ART at Iganga Hospital to assess crucial risk factors for very late ART initiation. All cases and controls were selected from Iganga Hospital because it was the unit with the best updated ART register - and also the only ART-providing unit until 2008.

The case definition was HIV-infected clients who started ART with a CD4 cell count of <50 cells/µl (very late initiators). The control subjects consisted of clients who started ART with a CD4 cell count of 50-200 cells/µl (late initiators). The cut-off margins were based on the Iganga hospital clinic observation where patients who start ART with a CD4 count below 50 cells/µl are prone to death, while those who initiate ART at a CD4 count below 200 cells/µl are prone to

immune reconstitution syndrome and always take a lot of time to resume normal functional ability. The margins were also based on studies in nearby settings where initiating ART at a CD4 below 50 cells/µl was associated with a higher risk of mortality (HR 1.006, 95% CI 1.003 to 1.008) (Smart, 2007) and the current WHO recommendation for starting ART at a CD4 cell count of < 350 cells/µl (WHO, 2009a). The cut-off points aimed at enabling us to classify other low counts, such as a CD4 count of 60 cells/µl, for example, which although <250 cells/µl (the recommended national threshold) is certainly not timely ART initiation.

All adult clients on ART in the hospital who enrolled for ART during the study period (January 2005 - December 2009) were eligible for the study. Given that the mean and median CD4 cell counts at initiation of ART for all clients were 122 and 126 cells/µl respectively (range 14-198 cells/µl) (DHO, 2009), these margins made all clients initiated on ART during the study period eligible. Clients on ART that were alive and of sound mental status were included in the study. Clients who initiated ART at the hospital before 2005 were excluded to reduce the risk of bias due to the unmet demand that had to be catered for during the first months of programme initiation in 2004. Clients in the PMTCT programme were also excluded because they had already been enrolled in another study at the same site (DHO, 2009).

The Fleiss formula (Fleiss, 1981) for sample size calculation was used under the following two assumptions: a) that the true ratio of cases to controls as observed from the hospital ART register was 40:60; and b) that exposure to pre-ARV care was similar for both cases and control subjects (50%). Exposure to pre-ARV care was used in sample size calculation because it is a very important explanatory variable for timely entry into HIV care (Lawn et al., 2010, Sanjobo et al., 2008). Thus at a power of 80%, with a target to detect a difference of absolute 16% as significant at 5% level, a minimum of 124 cases and 186 controls were needed for the study. To cater for clients who would withdraw consent or be difficult to trace for interviews, an additional 20% margin of subjects were recruited. In total 152 cases and 243 controls were recruited for the study.

The cases and control subjects were identified using systematic random sampling as described below. A chart review of the ART register at the hospital for the study period was done. From the review, all clients who satisfied the selection criteria above were identified and divided into cases

and control subjects in accordance with the CD4 count definitions given earlier. For each category (case vs control), a list with all clients' ART registration numbers was divided into serial pairs. Using simple random sampling, one of the two first numbers of each starting serial pair for each category was selected as the first client for the study, followed by every subsequent third client in each category until the desired sample size had been realised.

Trained research assistants then traced the clients for interviews using medical record information on address/place of living to seek informed consent. All the selected cases were subsequently interviewed, but 31 controls could not be interviewed either because they withdrew their consent for the interviews or could not be traced. Further scrutiny of records for the 23 who could not be traced showed that they were all males, and the 8 who withdrew consent were all women.Thus, the total number of interviewees enrolled in the study was 152 cases and 202 control subjects.

Semi-structured interviewer-administered questionnaires were employed for the study. Six research assistants who had previous experience in quantitative data collection from PLHIV within the Iganga-Mayuge demographic and health surveillance site interviewed the clients. The research assistants were trained for four days on the study aim, design and tools. The tools were pilot-tested at the nearest health centre IV offering ART. Experiences from the pilot study were discussed at an extra session together with the research assistants. Necessary changes were made to the tools and the assistants received additional guidance.

The data collected included individual/community-related factors associated with late/very late initiation of ART, such as the clients' age, gender, education, occupation, religion, number of people living in the household, marriage status and marital status. Other individual/community-related information included client-perceived barriers to timely ART, client perceptions and misconceptions about ARVs, CD4 count at ART initiation, and presence of family support. Health system-related data such as client-reported access to information on when to start ARVs after VCT, access to post-test pre-ARV care and waiting time for CD4 cell count results was also collected. Other health system-related data collected included waiting time between prescription and accessing ARVs (and if >1 month the reasons for waiting that long), clients' distance from the ARV centre, any care sought from other providers such as traditional/spiritual healers before

coming to the ARV centre, and reasons for their choice of service provider. The data were checked for consistency and completeness by the first and second authors (LM and TN) throughout the data collection period.

6.4 Data management

For studies I and III (qualitative studies) the entire data collection process was supervised and assessed by the first author of this thesis (ML), who is an indigenous public health physician, and the second author (XN), who is a social scientist with experience in qualitative research. Two indigenous research assistants chosen on the basis of their training and experience in carrying out social research moderated and took notes for the studies. The research assistants were trained for two days to become acquainted with the study aim, design and tools.

Role-plays were used to prepare the assistants for the different situations that were likely to arise in their interaction with the informants. Experiences from the role-plays were discussed at an extra session and further methodological guidance was given. All KIIs with health managers and providers were conducted in English, while the FGDs and the IDIs with PLHIV or their caretakers were conducted in Lusoga (the local language) and tape recorded to enable us to obtain the details and ensure an accuracy that we would not get from memory or field notes (Ryan *et al.*, 1996). The tapes were later transcribed and translated into English verbatim (for the FGDs and IDIs) by the interviewers. The authors listened to the tapes to confirm the credibility of the information. Data collection stopped when information relating to the topic guides revealed no new information. Data analysis was iterative, including reviews and discussions at different stages of data collection, and appropriate modifications were made in the tools to address emerging issues.

In studies II and IV all the completed questionnaires were checked for consistency and completeness by the first and second authors (LM and TN) during the study period. The checked questionnaires were then double-entered into the computer using Epi-Info version 2000 (Centers for Disease Control, Atlanta), and the two data sets were checked for discrepancies and further cleaned using analysis commands, lists and frequencies, and any range and consistence errors

identified were corrected. The data were then exported to STATA8 (STATA Corporation, College Station, Texas, USA) for univariate, bivariate and multivariate analysis.

6.5 Data analysis

Studies I and III (qualitative) were analysed using content analysis. The units of analysis were the interviews and FGDs. Content analysis can be manifest or latent; however, there is no clear line dividing the two since both deal with interpretation of findings, the only difference being a variation in the level of abstraction. While manifest content analysis refers to the analysis of visible obvious components (Kondracki *et al.*, 2002), latent analysis refers to the interpretation of the underlying meaning of the text (Downe-Wamboldt, 1992). Indeed, some authors prefer to describe the analysis as being close or not close to the text (Graneheim and Lundman, 2004). The content analysis used for these studies involved reading and reviewing texts of the entire interview back and forth to identify meaningful units in relation to the study aims (Morse and Field., 1995). The meaningful units were condensed into codes, categories and themes. During this process the researchers shared and debated the way each of them understood or coded the data until consensus was reached on the appropriate codes and themes.

In study II (RCT) data analysis was carried out in three stages. Stage 1 involved a description of baseline characteristics of the participants in the two arms to find out how comparable they were with respect to potential confounders such as age, education, and marital status. Chi-square and the *t*-test were used to test for any significant differences between the two arms for categorical and continuous data respectively.

Stage 2 involved bivariate analysis to establish the relationship between the different independent variables and the outcome variable. The risk ratios (RR) comparing uptake of pre-ARV care in intervention arm to the control arm, were computed as well as their 95% confidence intervals (CI). All variables where the association with the outcome variable had a *p*-value less than 0.2 were considered important for inclusion in the next stage of analysis. A stratified analysis in which the computed RRs for different levels of each independent variable were pooled using the Mantel-Haenszel RR was also performed. The Mantel-Haenszel RR was performed to adjust for

differences in risk ratios of uptake of pre-ARV at different levels of each independent variable. A Mantel-Haenszel procedure is robust and offers an elementary alternative of computing a common rate ratio to the earlier used maximum likelihood estimates.

Stage 3 was a multivariate analysis where different models assessing the independent effect of the intervention on uptake (primary outcome) of pre-ARV care were examined by controlling for different potential confounders. The multivariate analysis started by computing the RR generated by the intervention alone on uptake of pre-ARV care. Other models were then computed by cumulatively adding each of the independent variables that had been significant in stage two above until all the variables had been exhausted. The intervention was considered significant if the RR generated by the intervention alone did not change significantly for the different generated models.

In study IV (case-control study) we conducted univariate, bivariate and multivariate analysis using Stata. Following frequency distributions and cross-tabulations, the strength of association between variables was determined using odds ratios (OR) and 95% CI. For the bivariate analysis, cross-tabulations were run for each independent variable against the outcome variable (very late ART initiation). An independent variable was presumed to be significant if the cross-tabulation generated a *p*-value of <0.2. Multivariate analysis was also done to control for confounding and test effect modification. A logistical model was constructed to determine the best model for prediction of very late initiation of ART among ART clients. This process involved putting all plausible variables found to be significantly associated with very late initiation of ART among ART clients during the bivariate analysis into an initial model. The best model was thereafter generated using backward elimination and likelihood ratios to select the statistically significant variables.

6.6 Ethical considerations

The studies were approved by the Makerere University School of Public Health Higher Degrees Research and Ethical Committee and the Uganda National Council for Science and Technology. Study II (RCT) was registered by Current Controlled Trials Ltd C/O BioMed Central Ltd as ISRCTN94133652 at http://www.controlled-trials.com. The district authorities approved the

studies. The informants were told about the aims of the studies, their discretion to participate or withdraw at any time, and were assured that all information obtained from them would be kept confidential. The anticipated benefits of the studies such as an overall improvement in comprehensive HIV care for the individuals and the community were clearly explained to the participants. Anticipated harm caused by the studies, such as sharing the participants' HIV status with the research assistants at the follow-up health centre and/or the community support agents were also clearly explained to them. All the participants signed consent forms before any interviews could be commenced. To ensure confidentiality and minimise stigma the PLHIV were approached by the staff who attended to them during VCT.

6.7 Summary of methods

The methods used in the four studies and the timeframes are summarised in Table 5.

Table 5. Summary of methods and timeframe for the studies

Study	Setting	Design	Data collection method & study population	Data analysis	Year
1	Facility- and community-based	Qualitative-explorative	5 KIIs, 6 FGDs and 10 IDIs	Content analysis	2008
II	Facility- and community-based	RCT	Researcher administered multiple-response structured questionnaires (n=400)	Univariate, bivariate and multivariate Logistical regression	2009/ 2010
III	Facility- and community-based	Qualitative-explorative	20 IDIs and 10 FGDs	Content analysis	2008
IV	Facility- and community-based	Case-control-descriptive	Researcher administered multiple-response structured questionnaires (n=354)	Univariate, bivariate and multivariate Logistical regression	2010

7.0 RESULTS

7.1 Reasons for loss to follow-up of PLHIV under pre-ARV care (study I)

Reasons for dropping out of pre-ARV care that emerged from this study included inadequate counselling, competition from traditional/spiritual healers, transportation costs, waiting time, lack of incentives and gender inequality.

7.1.1 Inadequate counselling

Most informants indicated that the post-test counselling given to the newly screened PLHIV was inadequate. The overloaded staff acknowledged that they did not offer sufficient post-test counselling to the PLHIV about the importance of regular pre-ARV attendance. Some PLHIV even thought it was necessary to go to the clinic only when they fell sick:

> "Really often the patients are many and we are few ... we don't normally give them a lot of time for counselling, so sometimes maybe they don't understand and we have not followed them so we lose them" (Male health worker)

> "I only know I should go to the hospital when I have a problem. They did not tell us, are we supposed to go back? Anyway, they did not tell us" (Female (39), drop-out from pre-ARV care)

In contrast, the PLHIV who did not drop-out of pre-ARV care acknowledged the significance of adequate counselling:

> "I was encouraged to go back because of the counselling I received and the treatment that I always get from the clinic" (Female (38), adherent to pre-ARV care).

7.1.2 Competition from traditional/spiritual healers

Traditional/spiritual healers provided other forms of services in direct competition to the pre-ARV services from formal health providers. Some spiritual healers campaigned against some pre-ARV services, like cotrimoxazole prophylaxis, and portrayed the formal pre-ARV service as

useless since it could not cure HIV. The PLHIV perceived the healers as being affordable and easily accessible:

> "Some of the churches have even discouraged some of our patients from taking drugs. They tell them that when you take drugs you are showing God that you lack faith, yet the healing in church comes with faith." (Male, health worker)

> "Sometimes we go to traditional or spiritual people. Many of us we meet there. You know those people, you don't need a lot of transport to reach them. They also handle us well, give us advice and sometimes food or you can even sleep there if you are from far. I prefer them." (Female (33), drop-out from pre-ARV care)

7.1.3 Transportation costs and waiting time

Lack of transport was often mentioned as a barrier to regular pre-ARV attendance. Some PLHIV had difficulties affording transport costs to go to the units for the services unless they received collateral support. Others preferred to use the little money they had to purchase the cotrimoxazole locally rather than spending several times the cost on transport to get to the health units for the service. Another reason mentioned by the PLHIV for dropping out of pre-ARV care was the long waiting time at the clinics:

> "The problem I am seeing is transport ... at our church we organise for transport then take the members for testing and attending the clinic frequently." (Female informant, FGD)

> "I just buy cotrimoxazole and take. If you compare going to the clinic, staying in the long queue, you feel thirsty so it's better to use 500 and you buy cotrimoxazole instead of using 1500 Uganda shillings for transport." (Female (39), drop-out from pre-ARV care)

7.1.4 Lack of incentives

It was expressed that neither the health workers nor the respondents had fully grasped the benefits of offering or attending pre-ARV care. Some health workers did not want to prioritise PLHIV without obvious symptoms, given the high workload and few resources they had:

> "But really you know sometimes with the few resources we even ask ourselves do these people need us. They are doing work normally, so we prefer to give more attention to those on ART." (Female health worker)

On the clients' side, some PLHIV who had dropped out of the pre-ARV programme also expressed a lack of incentive to regularly attend pre-ARV care, since they felt healthy and able to work normally. They preferred to use their time and resources for other pressing needs:

> "Me, I am still healthy and doing my work. Why should I waste money on transport to get nothing? I rather spend it on food and fees for my children." (Female (39), drop out from pre-ARV care)

Others expressed the need for incentives such as bedding for PLHIV as a motivation for not dropping out of pre-ARV care, as in the following quote:

> "You should give incentives to the clients like us who have children, you should provide beddings. People get fed up when you go for meetings at the clinic and come home with nothing." (Female (22), drop-out from pre-ARV care)

7.1.5 Gender inequality

Some female informants expressed the fear of being beaten or divorced by their husbands as a reason why many women did not attend the pre-ARV clinic, even when they had tested and knew they were HIV-positive:

> "Also us we have a problem. If you go and test alone and find out that you are HIV-positive, we fear telling our husbands because if you tell him he will say that you brought the disease, so he will either beat you or send you away from your home." (Female informant, FGD)

Other females were denied access to pre-ARV care by their husbands out of ignorance. One man with four wives denied them access to pre-ARV care but kept telling them to take cotrimoxazole in the guise of preventing malaria:

> "Of course he had knowledge before but he could not tell us. I was so bitter about it because if I had known it early enough even the herpes zoster would not have come. He used to tell us to take cotrimoxazole every day, two of them. … He used to tell us that they treat malaria and one can never get sick." (Female (30), drop-out from pre-ARV care)

7.2 Effect of extended counselling on uptake of pre-ARV care (study II)

The study participant flow included a total of 400 newly screened PLHIV who were deemed eligible and enrolled for the study. In the intervention arm, 135/200 clients took up and returned for pre-ARV care and 65/200 did not return for pre-ARV care. In the control arm, 77/200 clients took up and returned for pre-ARV care while 123/200 did not return for pre-ARV care (Figure 5).

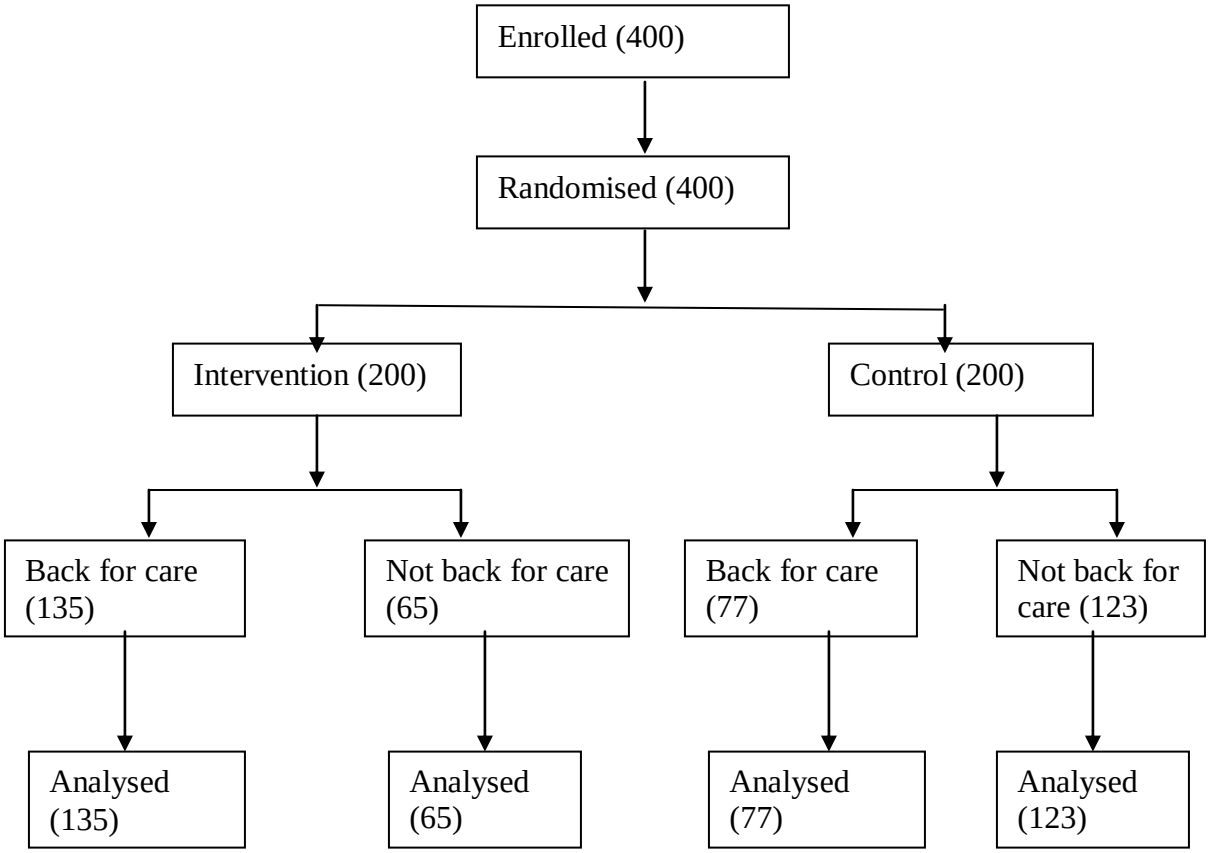

Figure 5. Participant flow diagram from enrolment to analysis.

The majority of the participants in both arms were comparable with regard to gender (p=0.75), age (p=0.48), education status (p=0.83), marriage status (p=0.90), occupation (p=0.62), distance to the centre (p=0.56) and number of people living in the household (p=0.23). There were, however, observed differences between the two arms with regard to pre-ARV awareness (p=0.008), religion (p=0.02) and marital status (p=0.02), although on further statistical analysis

these differences did not significantly influence the effect of the intervention on the outcome (Tables 6 and 7).

Table 6. Background characteristics in the two study arms in Iganga district (N=400).

Characteristics	Control (n=200) No. (%)	Intervention (n=200) No. (%)	Chi-square /*t* test (*p* value)
Centre			
Centre 1 (Busesa)	50 (25.0)	50 (25.0)	
Centre 2 (Iganga)	100 (50.0)	100 (50.0)	0.000 (1.00)
Centre 3 (Kiyunga)	50 (25.0)	50 (25.0)	
Sex			
Male	73 (36.5)	70 (35.0)	0.098 (0.75)
Female	127 (63.5)	130 (65.0)	
Age (years)			
18-24	39 (19.5)	29 (14.5)	
25-34	57 (28.5)	68 (34.0)	
35-44	58 (29.0)	56 (28.0)	2.480 (0.48)
45-70	46 (23.0)	47 (23.5)	
Education			
Low educated (none/primary)	130 (65.0)	128 (64.0)	0.044 (0.83)
Well educated (secondary +)	70 (35.0)	72 (36.0)	
Marital status			
Unmarried	82 (41.0)	61 (30.5)	4.799 (0.02)
Married	118 (59.0)	139 (69.5)	
Marriage status (for married people only)			
Monogamous	62 (52.1)	72 (51.8)	0.014 (0.90)
Polygamous	56 (47.9)	67 (48.2)	
Occupation			
Farmer	134 (67.0)	140 (70.0)	
Trader/business	48 (24.0)	40 (20.0)	0.964 (0.62)
Salary/wage earner	18 (9.0)	20 (10.0)	
Distance to unit (mean)	21.0 (SD=19.6)	22.0 (SD=21.1)	0.590 (0.56)
Household size (mean, SD)	6.1 (SD=3.8)	6.7 (SD=5.6)	1.200 (0.23)
Religion			
Christian	117 (58.5)	140 (70.0)	5.757 (0.02)
Muslim	83 (41.5)	60 (30.0)	
Pre-ARV awareness			
Aware	56 (28.0)	81 (40.5)	6.940 (0.01)
Not aware	144 (72.0)	119 (59.5)	

Both the bivariate and multivariate analyses were conducted using intention to treat, with a sample size of 200 participants for the intervention arm and 200 for the control arm. In the bivariate analysis, participants in the intervention arm were more likely to return for pre-ARV care compared to those in the control arm, with overall percentages of 38.5% and 67.5% for the control and intervention arms respectively and an unadjusted RR of 1.8 (95% CI: 1.4-2.1) (Table 7). Thus participants in the intervention arm were 80% more likely to take up pre-ARV care compared to those in the control arm.

The effect of the intervention remained significant after adjusting for the combined effect of each of the independent variables in stratified analysis, with a Mantel-Haenszel RR of pre-ARV uptake in the intervention arm compared to the control arm ranging from 1.6 to 1.8. Specifically, the Mantel-Haenszel RRs and their 95% CIs stratified for independent variables were as follows: recruitment health centre (Busesa) 1.8 (95% CI 1.4-2.1), sex (male) 1.7 (95% CI 1.4-2.1), age group (18-24 years) 1.8 (95% CI 1.4-2.2), education (low education) 1.8 (95% CI 1.4-2.2), marital status (unmarried) 1.8 (95% CI 1.4-2.1), marriage status (monogamous) 1.8 (95% CI 1.4-2.3), occupation (subsistence farmer) 1.8 (95% CI 1.4-2.1), distance to health facility (1-10 km) 1.8 (95% CI 1.4-2.0), number of people living in household with PLHIV (1-4) 1.8 (95% CI 1.4-2.2), religion (Christian) 1.7 (95% CI 1.4-2.1) and pre-ARV awareness (aware) 1.6 (95% CI 1.3-2.0). A test of homogeneity of the combined Mantel-Haenszel RR showed no significant difference among the strata. The result reaffirms the significant effect of extended counselling on uptake of pre-ARV care (Table 7).

Table 7. Uptake of pre-ARV care in both arms stratified for different categories of baseline characteristics in Iganga district (reference = control arm).

Variable	Control (N=200) (%)	Intervention (N=200) (%)	*p*-value, crude RR (95% CI)	Mantel-Haenszel RR
Recruitment centre				
Centre 1 (Busesa)	36.0	68.0	0.003 1.9 (1.3-2.9)	1.8 (1.4-2.1)
Centre 2 (Iganga)	39.0	68.0	<0.001 1.7 (1.3-2.3)	
Centre3 (Kiyunga)	40.0	66.0	0.013 1.7 (1.1-2.5)	
Sex				
Male	30.1	64.3	<0.001 2.1 (1.4-3.2)	1.7 (1.4-2.1)
Female	43.3	69.2	<0.001 1.6 (1.3-2.0)	
Age (years)				
18-24	41.0	65.5	0.050 1.5 (1.1-2.5)	1.8 (1.4-2.2)
25-34	35.1	64.7	0.002 1.8 (1.2-2.7)	
35-44	44.8	71.4	0.006 1.6 (1.2-2.2)	
45-70	32.6	68.1	0.002 2.0 (1.3-3.3)	
Education				
Low educated none/primary	40.0	69.5	<0.001 1.7 (1.4-2.2)	1.8 (1.4-2.2)
High educated (secondary +)	35.7	63.8	0.001 1.8 (1.3-2.6)	
Marital status				
Unmarried	39.0	68.5	<0.001 1.8 (1.3-2.4)	1.8 (1.4-2.1)
Married	38.1	66.9	<0.001 1.8 (1.4-2.3)	
Marriage status				
Monogamous	35.5	65.3	0.001 1.8 (1.3-2.7)	1.8 (1.4-2.3)
Polygamous	39.0	68.9	<0.001 1.8 (1.3-2.4)	
Occupation				
Farmer	40.3	65.0	<0.001 1.6 (1.3-2.1)	1.8 (1.4-2.1)
Trader	39.6	72.5	0.003 1.8 (1.2-2.7)	
Salary earner	22.2	75.0	0.008 3.4 (1.4-8.3)	
Distance to facility (km)				
1-20	43.3	72.8	<0.001 1.7 (1.3-2.1)	1.8 (1.4-2.0)
21-40	29.0	60.0	0.010 2.0 (1.2-3.6)	
41-90	33.3	61.0	0.016 1.8 (1.1-3.0)	
People in household				
1-4	41.2	66.2	0.005 1.6 (1.2-2.2)	1.8 (1.4-2.2)
5-9	36.4	76.3	<0.001 1.9 (1.4-2.5)	
10-45	40.9	71.4	0.049 1.7 (1.0-3.0)	
Religion				
Christian	43.6	75.0	<0.001 1.7 (1.4-2.2)	1.7 (1.4-2.1)
Muslim	31.3	50.0	0.024 1.6 (1.1-2.4)	
Pre-ARV awareness				
Aware	60.7	86.4	0.002 1.4 (1.1-1.8)	1.6 (1.3-2.0)
Not aware	29.9	54.6	<0.001 1.8 (1.1-1.8)	
Overall analysis	38.5	67.5	0.001 1.8 (1.4-2.1)	

In the multivariate analysis to control for potential confounders, all models generated did not change the adjusted RR obtained by the bivariate analysis between the intervention and the outcome RR of 1.8 (1.4-2.1) (Table 8).

Further analysis also showed that all participants in both arms were well informed about HIV transmission, prevention and AIDS-defining symptoms. The results also show that counselling was a major reason for participants coming back for care in the intervention arm (91.6%), compared to (8.4%) in the control arm (Figure 6). In addition, the majority of clients in the intervention arm (64.5%) who came back for pre-ARV care had disclosed their HIV status to their next of kin, compared to 34.5% in the control arm.

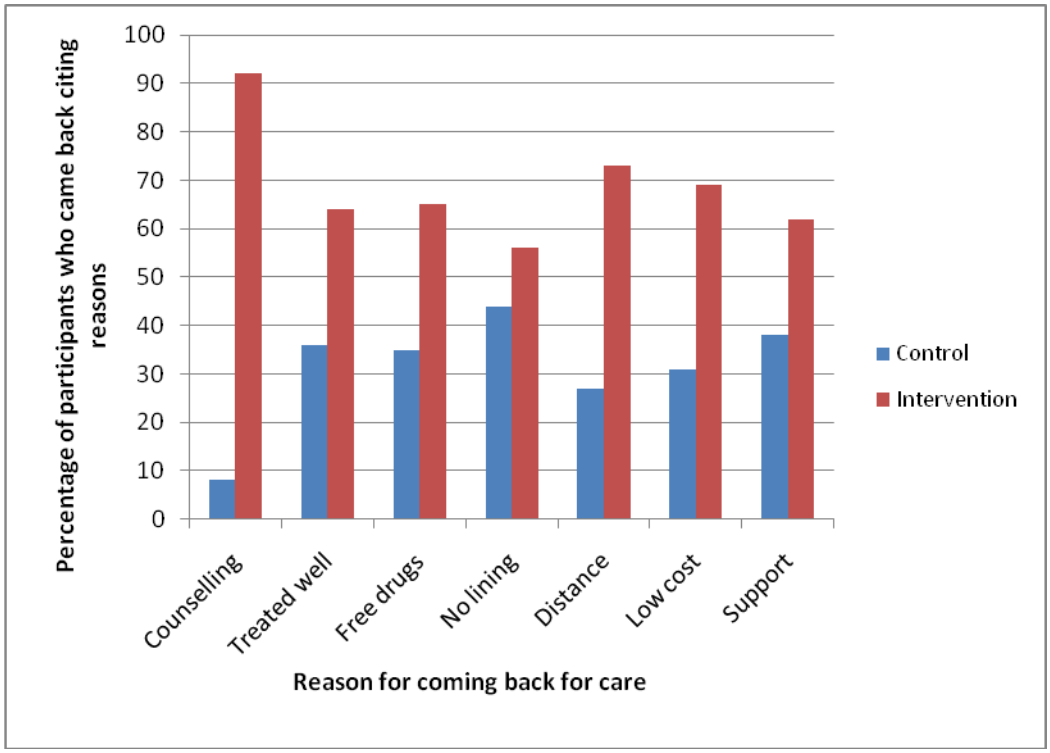

Figure 6. Study II (RCT) participants' reasons for coming back for care in both arms in Iganga district.

Table 8. Multivariate analysis to assess the effect of the intervention on uptake of pre-ARV care in Iganga district.

Model /variable (reference)	RR (95% CI)	*p* value
Model 1		
Intervention*	1.8 (1.4-2.1)	<0.001
Model 2		
Intervention*	1.7 (1.4-2.1)	<0.001
Sex (female/male)	1.1 (1.0-1.4)	
Model 3		
Intervention*	1.7 (1.4-2.1)	<0.001
Sex (female)	1.2 (1.0-1.4)	
Education(secondary/ primary)	0.9 (0.8-1.1)	
Model 4		
Intervention*	1.7 (1.4-2.1)	<0.001
Sex (female/male)	1.1 (0.9-1.4)	
Education (secondary/primary)	0.9 (0.8-1.1)	
Age group (base = 18-25 years)		
25-34	1.0 (0.7-1.2)	
35-44	1.1 (0.8-1.4)	
45-70	1.0 (0.6-1.3)	
Model 5		
Intervention*	1.7 (1.4-2.1)	<0.001
Sex (female/male)	1.2 (0.9-1.4)	
Education (secondary/primary)	0.9 (0.8-1.1)	
Age group (base = 18-25 years)		
25-34	0.9 (0.7-1.2)	
35-44	1.1 (0.8-1.4)	
45-70	1.0 (0.8-1.3)	
Centre 2 (Iganga Hospital/Busesa)	1.0 (0.8-1.2)	
Centre 3 (Kiyunga health subdistrict/Busesa)	1.0 (0.8-1.2)	
Model 6		
Intervention*	1.8 (1.4-2.1)	<0.001
Sex (female/male)	1.1 (0.9-1.4)	
Education (secondary/primary)	0.9 (0.8-1.1)	
Age group (base = 18-25 years)		
25-34	0.9 (0.7-1.2)	
35-44	1.1 (0.8-1.4)	
45-70	1.0 (0.7-1.3)	
Marital status (married/unmarried)	1.0 (0.8-1.2)	
Model 7		
Intervention*	1.8 (1.4-2.1)	<0.001
Sex (female/male)	1.2 (0.9-1.4)	
Education (secondary/primary)	0.9 (0.8-1.1)	
Marital status (married/unmarried)	1.0 (0.8-1.2)	
Occupation (trader/subsistence farmer)	1.1 (0.9-1.3)	
Occupation (salaried/subsistence farmer)	1.1 (0.8-1.2)	
Model 8		
Intervention*	1.8 (1.4-2.1)	<0.001
Sex (female/male)	1.2 (1.0-1.4)	
Education (secondary/primary)	0.9 (0.8-1.1)	
Marital status (married/unmarried)	1.00 (0.8-1.2)	
Occupation (trader/subsistence farmer)	1.1 (0.9-1.3)	
Occupation (salaried/subsistence farmer)	1.1 (0.8-1.4)	
Centre 2 (Iganga Hospital/Busesa)	0.9 (0.8-1.2)	

Centre 3 (Kiyunga health subdistrict/Busesa)	0.9 (0.7-1.2)	
Model 9		
Intervention*	1.8 (1.4-2.1)	<0.001
Sex (female/male)	1.1 (0.9-1.3)	
Education (secondary/primary)	0.9 (0.8-1.1)	
Marital status (married/unmarried)	1.0 (0.8-1.2)	
Occupation (trader/subsistence farmer)	1.0 (0.8-1.3)	
Occupation (salaried/subsistence farmer)	1.1 (0.8-1.4)	
Distance to facility in km (base = 1-20 km)		
21-40 km	0.8 (0.6-1.0)	
41-90 km	0.9 (0.8-1.1)	
Model 10		
Intervention*	1.7 (1.4-2.1)	<0.001
Sex (female/male)	1.2 (1.0-1.4)	
Education (secondary/primary)	0.9 (0.8-1.1)	
Marital status (married/unmarried)	1.0 (0.8-1.2)	
Occupation (trader/subsistence farmer)	1.0 (0.9-1.3)	
Occupation (salaried/subsistence farmer)	1.0 (0.8-1.3)	
People in house hold (base = 1-4)		
5-9	1.0 (0.8-1.2)	
10-45	1.1 (0.9-1.4)	
Model 11		
Intervention*	1.7 (1.4-2.0)	<0.001
Sex (female)	1.2 (1.2- 1.2)	
Education (secondary/primary)	1.2 (1.2-1.2)	
Occupation (trader/subsistence farmer)	1.1 (1.1-1.1)	
Occupation (salaried/subsistence farmer)	1.0 (1.0-1.0)	
Centre 2 (Iganga Hospital/Busesa)	0.8 (0.8-0.8)	
Centre 3 (Kiyunga health subdistrict/Busesa)	0.9 (0.9-0.9)	
Religion (Christian/muslim)	0.8 (0.6-0.9)	
Pre-ARV awareness (aware/not aware)	0.6 (0.5-0.7)	

*Statistically significant at 5% level.

7.3 Reasons for late initiation of ART (study III)

From this study we identified three overarching themes related to reasons for very late ART initiation among HIV-positive persons aware of their HIV status: *1. Weak health systems hindering timely initiation of ART,* categorised as "ARV stock-outs"; "inadequate pre-ARV care"; and "lack of staff confidentiality", *2. HIV/AIDS-related stigma hindering timely ART access,* categorised as "HIV/AIDS-related stigma" and "lack of social support", and *3. individual/community perceptions/misconceptions hindering timely initiation of ART,* categorised as "symbols of death" and "they cause cancer and infertility". These themes and categories are described below.

7.3.1 Health system barriers to timely initiation of ART

ARV stock-outs

The late initiators often reported that the inadequate supply or total lack of ARVs at the health facilities was a major demotivating factor, deterring new ART clients. Many witnessed that some eligible clients who were willing to start ART on time sometimes had to wait for months due to stock-outs of ARVs at the ART centres, making them feel discouraged and instead resorting to local herbs and traditional medicine:

> "Many times there are no ARVs at the centre. Some clients go and they are told they are ready for ARVs but they cannot start because the drugs are not there. We even wait for two to three months when the ARVs are not there. So this is discouraging." (Male (44), late initiator)

> "Anyway, sometimes the centres have no ARVs and I think this discourages some new clients who are ready to begin. For me I was lucky after counselling for ARVs the drugs were there, but I know some friends I took to the clinic to start ART and there were no drugs." (Female (41), timely initiator)

The inadequate supply of ARVs was echoed by community members in the FGDs, who reported that their relatives sometimes had been unable to start ART because there were no drugs available at the clinics:

> "Maybe the problems of the Global Fund led to this, but the reality is we are sometimes told there are no ARVs and staffs have to borrow here and there. That is also a big problem," (Female informant, FGD)

Inadequate pre-ARV care

Those who are diagnosed with HIV and are not yet eligible for ART due to good immune status are encouraged to go for routine monitoring of their immune status, i.e. pre-ARV care, in order to start ART on time before becoming symptomatic. Loss to follow-up during pre-ARV care was found to be crucial for late ART initiation. Many timely initiators had been under some kind of pre-ARV care which enabled them to be routinely monitored, and started on ART on time:

> "Well me after testing in 2005 we were told to come every three months, we used to come and they examine us, they even took my CD4 three times in two years, so it really helped me to be captured on time." (Male (33), timely initiator)

Conversely, many late ART initiators had not attended pre-ARV care or had sought care very late in the disease process, leading to delayed HIV diagnosis and late ART initiation:

> "Anyway, me, the problem really is because I went to the hospital late. I was first deceived that I had been bewitched so I delayed to come. I think it was my fault. Actually our friends who went early in their illness started ARVs on time, and by the way they look very good." (Male (35), late initiator)

Lack of confidentiality

Perceived lack of trust in some health workers was often mentioned by PLHIV as an important barrier to timely initiation of ART. Some late initiators reported knowledge of health staff sometimes discussing clients' HIV status in public, and stated that this was the main reason for them and other clients avoiding seeking care at the HIV clinics:

> "Anyway like me, I had sworn not to go to the hospital because I hear the staffs are rude and they keep pointing at you in public as someone on drugs which is bad, but later I went because I had nothing to do." (Female (24), late initiator)

> "The other problem is rumour-mongering by the staff. They talk about us in public telling people that we are on drugs so sometimes we fear to go there to keep our illnesses confidential." (Male (35), late initiator)

7.3.2 HIV/AIDS-related stigma and lack of social support inhibiting timely initiation of ART

HIV/AIDS-related stigma

HIV/AIDS-related stigma was found to have a major effect on seeking or accessing ART services on time. Some late initiators avoided any association with the ART clinic, since the public knew it was for PLHIV only. Others feared the negative perceptions associated with HIV/AIDS in the community. One account of a person living with HIV/AIDS described how they were coded by the community as the "walking dead":

> "You know, once people see you at the ART clinic they will obviously know you have AIDS, yet some of us don't want people to know for fear of discrimination. So sometimes it is better to keep away to remain with your respect." (Male (25), late initiator)

> "People point at you that you are a walking dead body, so naturally you fear to go. There is even one person who had all the signs of AIDS and I advised him to go and start treatment, but he feared to go and ended up dying." (Male (35), late initiator)

Lack of social support

Social support from the immediate family or the community in general was also vital for timely or late ART initiation. Some late initiators completely lacked a social network that could support them financially or in their decision-making for seeking early care:

> "Like me, I don't have support at all. Even my husband who should have helped me just accuses me of being a devil, a prostitute, and refuses to give me money to seek care. He says I brought the disease." (Female (39), late initiator)

In contrast, some timely initiators reported that the social support they had received from their immediate family had helped them seek services in time for ART:

> "Well for me my wife was very supportive. Even my brother they really encouraged me to seek help early after losing weight, so we went and my CD4 was 196, then I started ART." (Male (42), timely initiator)

7.3.3 Individual/community perceptions/misconceptions hindering timely initiation of ART

Symbols of death

Interviews revealed serious misconceptions about ARVs. Some late initiators perceived ARVs as drugs designed to kill, and thought that the Government used a particular type of ARVs labelled with a hoe and spade (a symbol of a grave) to kill PLHIV at a certain point in time after treatment started:

> "Also we knew the Government wants to reduce on the population. After some time they give you drugs with a hoe and spade (sign of a grave) to kill us. So it's better not to take the drugs. Me I came later because I had lost hope." (Female (31), late initiator)

> "It took me time to go for ARVs because people say that if you take ARVs for some time, at a certain point the workers give you those that are marked with a hoe and spade (symbol of death) and when that happens you know you are finished." (Male (25), late initiator)

"They cause cancer and infertility"

Apart from the perception that ARVs were drugs designed to kill, ARVs were also perceived to make PLHIV infertile or impotent, or predisposed to cancer. Many also believed that ARV drugs only give a brief life extension, since some people were known to have died shortly after ARV initiation. These misconceptions deterred many of those who had tested positive from seeking ART services in time:

> "Also, our experience is that these drugs cause cancer and they make people infertile. Others when they take them they live for a shorter period and then die, which is very discouraging." (Female informant, FGD)

7.4 Assessment of crucial risk factors for very late initiation of ART (study IV)

This study was an unmatched case-control study. A total of 354 clients (152 cases initiating ART very late at a CD4 count of <50 cells/µl and 202 control subjects initiating ART late at a CD4 count of 50-200 cells/µl) were interviewed for the study. The mean ages of the respondents were 38.0 and 41.4 years for the cases and controls respectively. The majority of both cases (82%) and controls (61%) were female. More cases (80.5%) than controls (59.1%) were unmarried and 84.5% of the very late initiators were subsistence farmers compared to only 40.9% among the controls. The majority of cases (70.2%) and none of the controls reported having experienced ARV stock-outs (Table 9).

Table 9. Univariate analysis of explanatory variables for ART initiation in Iganga, eastern Uganda (N=354).

Characteristics	CD4 <50 cells/µl (n=152)	CD4 50-200 cells/µl (n=202)
	No. (%)	No. (%)
Sex		
Male	28 (18.4)	78 (38.7)
Female	124 (81.6)	124 (61.3)
Mean Age	38.0 (SD=8.8)	41.4 (SD=8.9)
Education		
Well educated (secondary +)	54 (35.5)	178 (88.1)
Low educated (primary)	98 (64.5)	24 (11.9)
Marital status		
Married	30 (19.5)	82 (40.9)
Unmarried	122 (80.5)	120 (59.1)
Occupation		
Non-farmer	24 (15.8)	120 (59.1)
Subsistence farmer	128 (84.2)	82 (40.9)
Distance (km) to health facility (mean)	17.9 (SD=14.6)	14.6 (SD=15.2)
ARV supplies experienced by patients		
Stock-outs	107 (70.2)	00 (00.0)
No stock-outs	45 (29.8)	202 (100.0)
Confidence in staff		
Present	00 (00.0)	202 (100.0)
Absent	152 (100.0)	00 (00.0)
Family support		
Available	28 (18.4)	122 (60.4)
Not available	124 (81.6)	80 (39.6)
Pre-ARV care		
Attended	38 (25.0)	148 (73.3)
Not attended	114 (75.0)	54 (26.7)
Traditional/spiritual care-seeking before ART		
No	46 (30.3)	178 (88.1)
Yes	106 (69.7)	24 (11.9)

Client-reported barriers to timely initiation of ART included mainly ARV stock-outs, competition from traditional healers, inadequate pre-ARV care and lack of family support, as reported by the very late initiators (Figure 7).

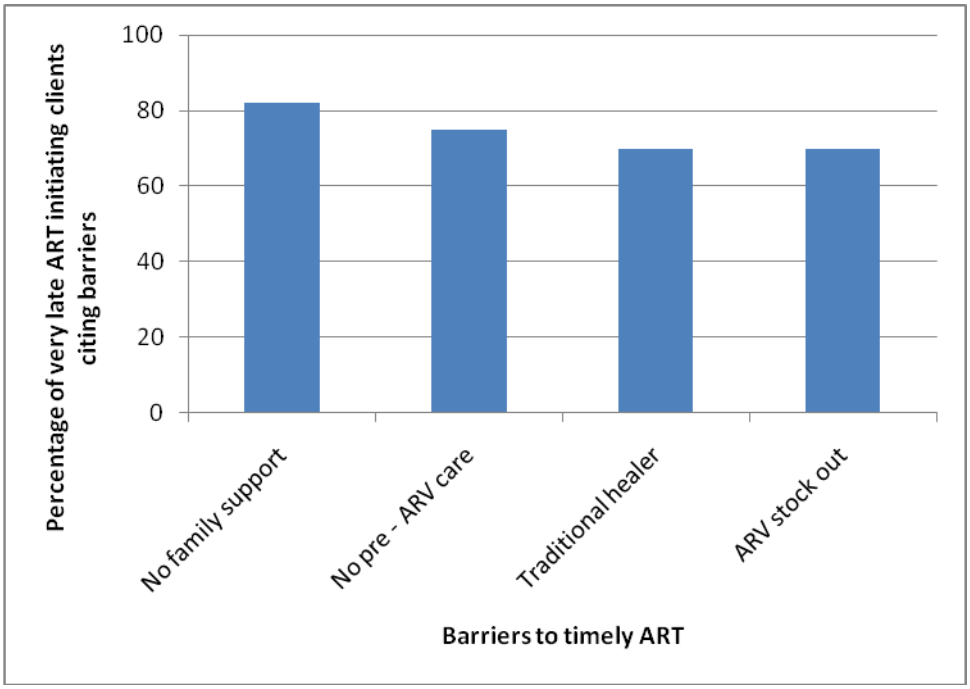

Figure 7. Client-reported barriers to timely initiation of ART in Iganga district.

Other barriers for timely initiation of ART were personal characteristics such as being male, being a subsistence farmer or being younger. Very late initiators reported seeking care from traditional/spiritual healers because they perceived the healers as being accessible, nearer, less expensive, more holistic and better-quality care providers than the public ART services (Figure 8).

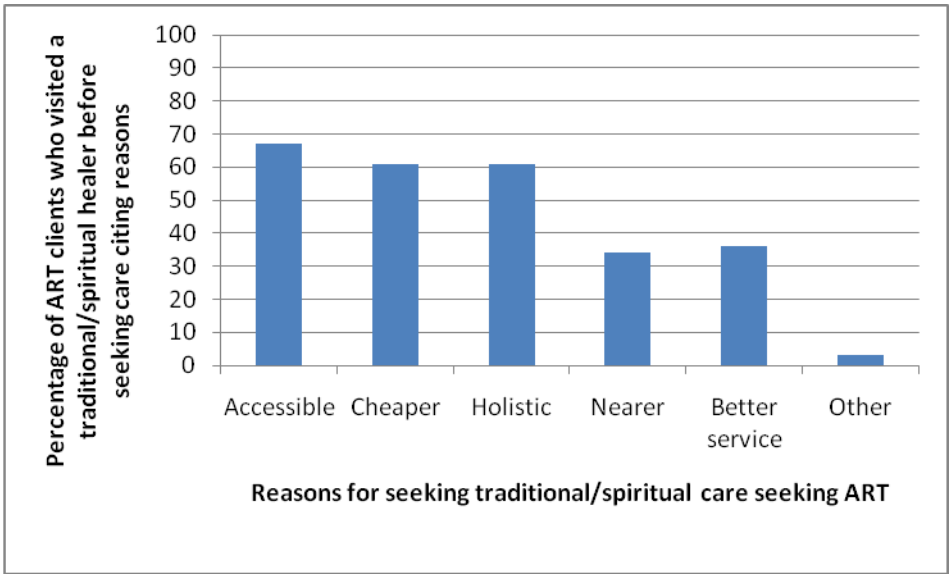

Figure 8. Client reasons for visiting traditional/spiritual healers before seeking ART care in Iganga district,

The bivariate analysis established that very late initiation of ART was a function of both individual/community-related factors as well as important health system-related factors.

7.4.1 Individual/community-related factors

Females were three times more likely to initiate ART very late compared to males (OR 2.8; 1.7-4.6). Older clients had a lower risk of initiating ART very late compared to young clients (OR 0.9; 95% CI 0.8-0.9). Low educated clients were almost 14 times more likely to initiate ART very late compared to clients who were well educated (OR 13.5; 95% CI 7.8-23.1). Clients who were unmarried were five times more likely to initiate ART very late compared to those who were married (OR 5.3; 95% CI 3.2-8.6). Subsistence farmers were eight times more likely to initiate ART very late compared to non-farmers (OR 7.8; 95% CI 4.7-13.1). Clients who lacked family support were seven times more likely to initiate ART very late compared to those who had family support (OR 6.7; 95% CI 4.1-11.1) (Table 10).

7.4.2 Health system-related factors

Clients who had reportedly not attended pre-ARV care were eight times more likely to initiate ART very late compared to those who had attended pre-ARV care (OR 8.2; 95% CI 5.1-13.3). In addition, clients who had reportedly sought care from traditional/spiritual healers before seeking formal ART care were 17 times more likely to initiate ART very late compared to those who did not seek prior traditional/spiritual care (OR 17.1; 95% CI 9.1-29.6) (Table 10).

The variables that remained significantly associated with very late ART initiation in the multivariate analysis included being female (adjusted OR (AOR) 0.4; 95% CI 0.2-0.8), increase in age as a continuous variable (AOR 0.9; 95% CI 0.8-0.9), and living nearer the health facility (AOR 0.1; 95% CI 0.1-0.5), all of which were protective against very late ART initiation. The others were subsistence farming (AOR 6.3; 95% CI 3.1-13.0), lack of family support (AOR 3.3; 95% CI 1.6-6.6), lack of pre-ARV care (AOR 4.6; 95% CI 2.3-9.3), and having sought previous care from traditional/spiritual healers for AIDS-related symptoms (AOR 7.8; 95% CI 3.7-16.4) (Table 10).

Table 10. Factors associated with very late initiation (CD4 <50 cells/µl) of ART in Iganga, eastern Uganda, (N=354).

	Bivariable		Multivariable	
Variable	***p* value**	**Crude OR (95% CI)**	***p* value**	**AOR (95% CI)**
Sex				
Male		1		1
Female	<0.001	2.8 (1.7 - 4.6)	0.010	0.4 (0.2 - 0.8)
Age (continuous)*	0.001	0.9 (0.8 - 0.9)	0.001	0.9 (0.8 - 0.9)
Education				
Well educated (secondary +)		1		1
Low educated (primary)	<0.001	13.5 (7.8 – 23.1)	0.080	2.2 (0.9-5.1)
Marital status				
Married		1		1
Unmarried	<0.001	5.3 (3.2 - 8.6)	0.120	1.8 (0.8 -3.7)
Occupation*				
Non-farmer		1		1
Subsistence farmer	<0.001	7.8 (4.7 - 13.1)	<0.001	6.3 (3.1-13.0)
Distance to health facility (km)*				
1-10		1		
11-20	0.220	1.4 (0.8-2.5)	<0.001	0.1 (0.1-0.5)
21-30	0.010	2.3 (1.2-4.3)	0.001	0.1 (0.0-0.4)
31-65	0.060	1.8 (1.0-3.2)	0.024	0.3 (0.1-0.8)
Family support*				
Available		1		1
Not available	<0.001	6.7 (4.1 - 11.1)	0.001	3.3 (1.6 - 6.6)
Pre-ARV care*				
Attended		1		1
Not attended	<0.001	8.2 (5.1 - 13.3)	<0.001	4.6 (2.3 - 9.3)
Traditional/spiritual care-seeking before ART*				
No		1		1
Yes	<0.001	17.1 (9.1 - 29.6)	<0.001	7.8 (3.7 - 16.4)

* Statistically significant at 5% level.

8.0 DISCUSSION

8.1 Discussion of main findings

In this thesis we highlight that loss to follow-up of PLHIV in transit from HIV counselling and testing to pre-ARV care and subsequent initiation of ART (Figure 2) is not just a function of the will of the PLHIV, but a complexity of intertwined factors ranging from a deficient health system to individual/community misconceptions about HIV care. We also demonstrate that a low-cost intervention - extended counselling through use of available staff with basic training in counselling skills - combined with home visits by community network support agents, can improve uptake of pre-ARV care and status disclosure (paper II), which may improve timely initiation of ART. The main health system factors involved include inadequate post-test counseling, lack of pre-ARV care for newly screened PLHIV, competition from traditional and spiritual healers, ARV stock-outs and perceived lack of staff confidentiality (papers I, III and IV). The individual/community perceptions or misconceptions that hinder regular pre-ARV care or timely initiation of ART include stigma and associated lack of family/social support, gender inequality (particularly affecting women) and misconceptions about ARVs (papers I, III and IV). Adequate post-test counseling at the time of VCT and follow-up care that is accessible and affordable by the PLHIV (I, II) are thus central to uptake and retention of PLHIV under pre-ARV care. Retention of PLHIV under pre-ARV care (III, IV) is also vital for timely initiation of ART (Figure 2).

In the socio ecological model, the will of the PLHIV to seek care falls under the individual level, the deficient health system falls under the organizational and public policy level, while community misconceptions about HIV care fall under the interpersonal, organizational and community levels. The low-cost intervention cuts accross all the levels of the model (Figure 1). The findings therefore illustrate the importance of the relationship between the person (PLHIV) and other levels of their environment (partner, family, community, social networks and health system goals and functions), in influencing access to HIV care and health-seeking behaviour (Figure 1). Therefore , enhancing uptake of pre-ARV care, minimising loss to follow-up of PLHIV and improving timely initiation of ART will require focus on several levels: the PLHIV, the deficient health system, the community and other social environmental factors to develop comprehensive interventions that systematically target mechanisms of desired change at each level of influence (McMurray, 2006, McLeroy et al., 1988,

Stokols et al., 1996, Sallis JF and Owen N, 2002, Sallis and Glanz, 2006, Fleury and Lee, 2006, Moore, 2001).

8.1.1 Health systems-related factors

Inadequate post-test counselling

Inadequate post-test counselling was one of the reasons for loss to follow-up of PLHIV during pre-ARV care (paper I). Newly screened PLHIV were not given adequate information about the importance of pre-ARV care or the dangers of dropping out of pre-ARV care. The PLHIV expressed a lack of awareness of why and when they should return for pre-ARV care, which is likely to have contributed to the high dropout rate during pre-ARV care (Figure 2). The staff in the clinic also confessed that because of the high workload, they did not have enough time to educate the newly screened PLHIV about the importance of regular pre-ARV care.

The importance of counselling as a prerequisite for retention of PLHIV in HIV care programmes has been highlighted by other studies in Africa and Asia (Hardon et al., 2007, Chesney, 2000, Coetzee et al., 2004, Sanjobo et al., 2008). Much as the WHO provides standardised post-test counselling guidelines for PLHIV, in many low-income settings the quality and quantity of post-test counselling is poor, partly because the staff are overloaded or have not been trained in basic counselling skills (WHO/UNAIDS, 2005). Improving post-test counselling would necessitate the health system overcoming the challenge posed by staff workload or lack of counselling skills which fall under the organizational and public policy level of the SEM. This may help in enhancing awareness about the importance of regular pre-ARV care for the PLHIV (under the individual level of the SEM), and hence minimize those lost to follow-up. The SEM recognises that behaviour change is expected to be maximised when individuals are motivated and educated to make useful health choices (WHO, 1986, McMurray, 2006).

Lack of pre-ARV care

Lack of pre-ARV care was related to late ART initiation (papers III and IV). Regular attendance of pre-ARV care enhances routine assessment of a patient's eligibility for treatment and hence timely ART initiation (Figure 2). As demonstrated by previous research from resource-poor high-prevalence settings in Uganda, South Africa and Asia, the finding highlights the importance of early HIV

diagnosis, adequate post-test counselling and follow-up for PLHIV in pre-ARV care to ensure timely initiation of ART (Chesney, 2000, Sanjobo et al., 2008, USAID, 2009, Lawn et al., 2010, Kigozi et al., 2009).The lack of pre-ARV care could be attributed to late presentation/late diagnosis and hence failure to benefit from the advantages of early diagnosis such as post-test counselling and routine monitoring of eligibility for ART (Losina et al., 2010, Long, 2008).

Lack of pre-ARV care could also be related to factors that go beyond the individual will of the PLHIV (individual level of the SEM) - to the health system and community deficiencies in general (organisational, community and public policy levels of the SEM). Long distance to the health facility, transport costs, hunger, waiting time and stigma have, for example, been established as important barriers to access and adherence to HIV care in resource-poor settings (Hardon et al., 2007, Maskew et al., 2007). The health system therefore needs to adopt comprehensive HIV care approaches that go beyond the individual will to take an HIV test and attend pre-ARV care to also address associated gaps in the community and the health system itself. Comprehensive home- based HIV care from VCT to ART which addresses some of these gaps has, for example, been found to improve access to and retention of PLHIV in HIV care programmes, the HIV-related stigma and involved high costs notwithstanding (Weidle Paul J et al., 2006, Mukherjee et al., 2006).

The role of low-cost interventions (II)

Study II demonstrates that if newly screened PLHIV receive specialised counselling by staff who have received low-cost training in basic counselling skills, combined with home visits by community support agents, they are up to 80% more likely to take up pre-ARV care (paper II). The study further indicates that extended counselling may also help clients overcome other barriers to comprehensive HIV care in resource-poor settings (such as high transport costs), as well as enhance social support by encouraging status disclosure. The finding meets the WHO recommendation for effective interventions that are simple and relatively inexpensive to improve the quality of life of PLHIV, prevent further transmission of HIV, delay progression of HIV disease and prevent mortality by increasing access to care through health facilities and community outreaches (Nakanjako et al., 2009, WHO et al., 2008).

Community support agents (who fall under the interpersonal, organizational and community levels of the SEM), may thus be used to supplement the efforts of the already overloaded staff at ART clinics and make the health system more efficient in providing pre-ARV care to the PLHIV. The intervention is therefore likely to create the impetus for routine pre-ARV care for the poor and most vulnerable PLHIV and subsequently ensure timely access to ART (Figure 2).

The direct financial cost for the training in basic counselling skills was only US $20 per staff member, a sum that should be comparable in other rural contexts in SSA. In similar settings that are able to mobilise volunteer community support agents, such an intervention would therefore probably be feasible. The authorities would, however, need to address other important system deficiencies such as stock-outs of HIV testing kits and cotrimoxazole, and the poor staff attitudes towards clients that are common in similar settings (MOH, 2009).

Competition from traditional/spiritual healers

Competition from traditional/spiritual healers was related to loss in transit of PLHIV during pre-ARV care (paper I), and is a crucial risk factor for very late initiation of ART (paper IV). The healers undermined formal HIV care as they provided alternative and competing HIV care services. Many ART-eligible clients reportedly sought care late (Figure 2) because they had been delayed by first seeking traditional/spiritual healing, which they perceived as being more accessible, cheaper, holistic and of better quality compared to the established ART centres (paper IV).

Other studies indicate that the influence of such healers on people's health-seeking behaviour is not unique to Iganga but also many other resource-poor settings (WHO et al., 2008, Taylor et al., 2008, Burnett et al., 1999, Baguma, 1996, Kaboru, 2008, Ritzenthaler, 2005, Homsy and King, 1996, Ochai, 2008, Tate et al., 2010, Kusimba et al., 2003). Available evidence indicates that four out of every five PLHIV in the rural developing world visit and use traditional/spiritual healing (Frimpong JY and Oppong, 2004, Prometra, 2008, UNAIDS, 2000).

Studies by the (WHO, 2004, Myron, 2002, Robert, 2005) also show significant evidence that many PLHIV seek spiritual healing at all stages of the HIV/AIDS cycle from VCT to ART. Although many traditional and other complementary healers in Uganda remain unaffiliated to the formal health

system, approximately 60% of Uganda's population seeks care from them before visiting the formal health sector (MOH, 2009). The healers have been confirmed to provide client-centred, personalised health care that is culturally or spiritually appropriate, holistic and tailored to meet the needs of and expectations of the patients (UNAIDS, 2000). Because traditional healers are culturally/spiritually close to the patients, they easily communicate to patients about disease and other related social issues, which is an important factor in the treatment of STIs (UNAIDS, 2000).

In the SEM, traditional/spiritual healers fall under the organizational and community levels. Since they seem to have a big influence on health-seeking behaviour for PLHIV, policy makers could consider integrating them into comprehensive HIV care at the public policy level of the SEM as well. This may be achieved through sensitising and support-supervising the healers to provide some HIV care services, like distributing cotrimoxazole to PLHIV. Such collaboration has been found useful in counselling and herbal research in Uganda and Zambia (Burnett et al., 1999, Kaboru, 2008). However, adequate training and supervision of the healers needs to be emphasised to ensure that quality of care is not compromised.

Timely ART initiation could be improved by making ART services more affordable, accessible and user-friendly through peripheral units and trained, supervised lay workers, so that the services are more attractive than traditional/spiritual healers. Such interventions have been found effective in clinical studies in Africa, where ART delivery models for nurses and non-clinical staff aimed at reducing the workload of physicians and treatment and monitoring delivered through peripheral health centres or through home visits have achieved better adherence and been more cost-effective than ART delivery at hospitals (Jaffar et al., 2005, Jaffar, 2009).

ARV stock-outs

A major health system-related factor for very late initiation of ART was the irregular supply of ARVs (papers III and IV). At times when ARVs were out of stock, some clients who had been counselled to start ART reportedly had to wait for a long time before they could start treatment. The demotivation caused by lack of ARVs could have been a main gateway for many PLHIV getting lost in transition before actually initiating ART (Figure 2). This finding supports other reports on ART-eligible clients

failing to access ARVs or doing so too late due to stock-outs in Uganda (Nakkazi, 2009, Nakanjako et al., 2009, Hasunira and Muhinda, 2009, Avert, 2010, Jirair, 2010).

The stock-outs of ARVs could have been due to an inefficient supply and procurement chain and/or a poor data management system that undermined forecasting the quantities of drugs required. ARV stock-outs could also partly have been due to shortfalls in funding for procuring the drugs, which is a common occurrence in Uganda due to shortfalls in health care financing for the public health sector (MOH, 2009).

Stock-outs of essential drugs due to insufficient supply chains and shared responsibilities between key actors that may be difficult to influence at facility level alone are common in SSA (UNAIDS/WHO, 2005, Kiwanuka et al., 2008). There is need, however, to ensure procurement planning at facility, district and national level (figure 1) for all drugs and supplies needed to improve comprehensive HIV care. Ensuring availability of ARVs to communities at all times is vital for encouraging service utilisation (WHO, 2003c). Timely and appropriate provision of drugs as a way of improving quality of care was also found significant in sociocultural studies to explain timely and appropriate use of health facilities for febrile illnesses in Tanzania and Malawi (Dillip et al., 2009, Chibwana et al., 2009).

Lack of staff confidentiality

Perceived lack of confidentiality of the staff by the PLHIV was mentioned as a barrier to accepting and seeking HIV care services (paper III). Confidentiality is a crucial aspect in all sorts of patient management, but in particular for PLHIV. Many PLHIV have not even disclosed to their partners, social networks or employers that they are HIV-positive or on treatment because of the stigma associated with ARVs, which may be as strong as the stigma associated with the actual infection. Our finding is supported by other studies from Uganda, Ethiopia and Pakistan, where perceived provider confidentiality was an important factor for determining health-seeking behaviour and drug adherence (Gusdal et al., 2009, Mbonye AK et al., 2009, Shaikh, 2008, Shaikh et al., 2008).

If true, however, this perception raises major concerns regarding the ethical conduct of many health care providers and the serious effects of confidentiality breach on health-seeking behaviour of

PLHIV. Policy makers and providers therefore need to ensure that policy guidelines with regard to client privacy and confidentiality are disseminated and adhered to by the attendant staff.

Social mobilisation for PLHIV and the community in general through the local media or local leaders should be done to assure clients that their illnesses will be kept as confidential as possible. The newly screened PLHIV also need reassurance at the time of VCT that their HIV sero status or treatment will not be disclosed to anyone without their consent. Such interventions that go beyond the individual PLHIV but also include the health care delivery system and their environment are likely to be successful in improving provision and health seeking for comprehensive HIV care (DiClemente *et al.*, 2004; DiClemente *et al*., 2005; Campbell *et al*., 2007; Sallis & Glanz, 2006; Sallis & Owen, 2002; CARE, 2010).

8.1.2 Individual/community factors hindering timely initiation of ART

Lack of social support, gender inequalities and misconceptions about ARVs were found to be barriers to timely initiation of ART in this study.

Lack of social support

PLHIV are faced with a broad array of needs related not only to treatment of HIV, but also emotional, material, nutritional, financial, spiritual and psychosocial support. In this study, lack of social support was reported as a barrier to timely initiation of ART and associated with very late initiation of ART (papers III and IV). The significance of social support as a prerequisite for appropriate HIV care has been reported by other studies in South Africa, Zambia, Malawi, India and Brazil (Carvalho et al., 2007, Birbeck et al., 2009, Bwirire et al., 2008, Feucht et al., 2007, Makoae et al., 2008, USAID, 2009).

Social support helps in accessing ART services, and understanding behavioural and routine changes in the schedule of PLHIV such as monthly or quarterly visits to the ART centre for pre-ARV care or ARVs. It also discourages HIV/AIDS-related stigma (paper III). On the other hand, inadequate social support predisposes PLHIV to, among others, unemployment, poverty, and lack of awareness of or access to vital information and communication about the care. Inadequate social capital has been

established as a vital predictor for late or poor health-seeking behaviour by other studies in low- and medium-income countries (Kigozi et al., 2009, Krawczyk et al., 2006, Diero et al., 2006, Severe et al., 2005, Wood et al., 2003, Bakeera et al., 2009, Bakeera et al., 2010, Ahmed F et al., 2005).

The social support may be provided by the intimate partners of PLHIV, the immediate family, close friends, relatives, employers, spiritual leaders or other social networks at the interpersonal and organizational levels of the SEM. Thus, while the provision of free ARVs has increased rapidly in Uganda, the Ugandan Government and global funding agencies need to address the unmet need for social support to PLHIV proportionately in order to positively influence timely and appropriate HIV care. Indeed, the Government of Uganda and its partners has made social support a thematic area for improving comprehensive HIV care in the country in its National HIV & AIDS Strategic Plan 2007/8-2011/12 (UAC, 2007, UAC, 2010, URCS, 2008, Population-Council., 2010).

Enhancing the social support for PLHIV will require focus on both the individual and socio-environmental factors to develop comprehensive interventions that systematically target mechanisms of change at each level of influence (McMurray, 2006; Stokols *et al.*, 1996; Fleury & Lee, 2006; Sallis & Owen, 2002; McLeroy *et al*., 1988; Sallis & Glanz, 2006). Several authorities also emphasise that the concept of seeking and accessing health care must be a shared responsibility between individual, organisational, community and public policy structures (Shaikh et al., 2008, Moore., 2001).

Misconceptions about ARVs

Misconceptions/negative perceptions about ARVs, container labels and PLHIV were found to be deterrent to timely ART initiation (paper III). Some PLHIV negatively perceived ARVs as drugs designed by Government to kill and control population growth, or causing cancer or infertility. Negative perceptions and dangerous misconceptions have been identified as barriers to HIV diagnosis and ARV treatment by other studies in Uganda, Tanzania and other resource-poor settings (Atuyambe et al., 2008, Nicholson et al., 2006, Micek et al., 2009, Chomat et al., 2009, Ezekiel et al., 2008, Ezekiel et al., 2009).

Previous studies from Africa, South America and Asia have also established that misconceptions about drugs or other care are vital in terms of health-seeking behaviour (Ezekiel et al., 2009, Bonjour et al., 2008, Banerjee and Mattle, 2005). The misconceptions about ARVs could have been a function of lack of knowledge and awareness about HIV or HIV care-seeking concepts and the branding of ARV drug containers (Agnew-Blais *et al*., 2008).

Thus although there is apparent knowledge about HIV and ART in Uganda, many people - especially in rural settings - still have negative misconceptions about several elements of comprehensive HIV care (MOH, 2006). Policy and practice should therefore be driven towards sending out messages that address the misconceptions about ARVs to enhance acceptance of ART. Great care must be taken to pilot the disseminated information, if possible in all the local languages, to make sure it is accurate and to avoid misinterpretation.

Gender inequality

Gender inequality was reported as a reason for loss to follow-up of PLHIV during pre-ARV care (paper I). The case of a man denying his four wives access to pre-ARV services gives a contextual image of what may happen in similar family set-ups. Studies in Africa and Asia have also found that women cannot access STI services like VCT because of financial constraints, lack of information and lack of decision-making powers as to when and where to seek the care (WHO, 2003b, Voeten et al., 2004, Manhart et al., 2000). Other studies have also established that women are disadvantaged compared to men in accessing health care in general (Turmen, 2003, Wingood et al., 2007, Skinner and Mfecane, 2004, Mrisho et al., 2009, USAID, 2009).

In paper IV, however, women were 60% less likely to start ART very late compared to men after adjusting for other confounders. We deliberately excluded females diagnosed with HIV/AIDS early due to pregnancy and initiated on ART through the PMTCT programme so that we could look at all other women. The finding can probably be explained by the stronger stigma and denial seen among men in relation to AIDS-related symptoms in resource-poor settings, as reported elsewhere (Larsson *et al*., 2009). The socio-ecological context of the finding is that policies that address men's stigma and women's disadvantages in decision making and care seeking for HIV care and other health-

related problems need to be emphasised at all levels of the ecological tree, from the personal and interpersonal to organisational and community perspectives (Moore, 2001).

8.2 Methodological considerations

8.2.1 Papers I and III

For papers I and III (qualitative papers) the research team tried to take all appropriate measures to ensure that the aims for which the two studies were conducted were achieved. The research team was multidisciplinary and included a public health physician (LM) who has managed HIV patients in the pre-ARV and ART clinics for at least 10 years. The other (XN) was a social scientist with a lot of experience in carrying out qualitative research with regard to HIV care in the research setting. The research assistants were native to the area, understood the local language and had been involved in conducting qualitative research in the study setting. The team was thus well prepared in understanding the contextual aspects of the topics under study (Dahlgren *et al.*, 2004).

The team collected data from a variety of sources, including staff who worked at the clinics, the PLHIV themselves and their relatives or caretakers. We also triangulated our data collection methods (KII, FGDs and IDIs), which helped us to check for consistency and contradictions inside and across the groups and interviewees (Rice P L and Ezzy, 1999, Berg, 2001). During data collection the team spent long periods of time with the interviewees in the field which, enabled us to understand the reality of our respondents. LM and XN initially coded the data independently and later sat to agree on the coding. The team also presented the scripts and agreed coding to peers (PG, TNM, SP, AME and FWM) who were not part of the data collection process to generate consensus on the coding process (Dahlgren *et al.*, 2004). We therefore feel that the content analysis employed for these studies has contributed appropriate in-depth analysis for the purpose of the studies.

There were, however, some shortcomings. We did not observe how post-test counselling is conducted at the units. This could have helped us assess the quality of the counselling and its contextual relationship with drop-outs from pre-ARV care. Similarly, conducting FGDs with friends, relatives or caretakers of PLHIV instead of the PLHIV themselves was also a limitation, since it generated collateral information which sometimes needed validation. However, the collateral information from

the caretakers helped us understand the sociodynamic and contextual issues related to loss to follow-up of PLHIV under pre-ARV care and late initiation of ART.

8.2.2 Papers II and IV

Randomisation and masking

In paper II the description of the intervention by background characteristics shows that randomisation of the study participants worked well, and that the association between the intervention and the outcome variable (uptake of pre-ARV care) may not have been affected by participant assignment bias. All the staff members who conducted the counselling at the different centres were from the same units and had worked together in these units for a long time; thus complete decontamination between staff was hard to ensure, but genuine efforts were made during pre-trial training to inform them about the importance of avoiding discussing the intervention. It was also impossible to entirely ensure that the participants did not share information about the trial between themselves, although this is unlikely given the sensitivity of the topic and the high stigma still associated with HIV in the community (Roura et al., 2009, UAC, 2007).

Follow-up and unpacking the intervention

The intervention did not involve following up of the community support agents. It was therefore difficult to ascertain the quality and quantity of counselling they provided to the participants during follow-up visits in their homes. It was equally hard to ascertain whether it was the initial post-test counselling provided by the staff at the unit in the intervention arm, and/or the follow-up counselling provided by the community support agents that encouraged participants to come back for pre-ARV care. Unpacking the intervention could thus be a subject for further research.

Selection bias

In paper IV the use of CD4 count as a measure for very late initiation of ART influences the interpretation of our results, because a low CD4 count does not automatically translate into late disease or symptomatic disease but varies somewhat among individuals. The decision to use CD4 counts to classify case status as well as the low cut-off margins used was made to facilitate comparisons with other studies taking the current WHO classification of late presentation as a

standard. The decision was also based on our clinical observations and other studies performed in Uganda about the prognosis of very late ART initiators. All adult clients on ART in the hospital who enrolled for ART during the study period (January 2005 - December 2009) were eligible for the study. Given that 40% of the clients initiated on ART in Iganga district between 2004 and 2009 had a CD4 cell count of <50 cells/µl and that the mean and median CD4 cell counts at initiation of ART for all clients were 122 and 126 cells/µl respectively (range 14 -198 cells/µl) (DHO, 2009), these margins made all clients initiated on ART during the study period eligible.

The selection criteria excluded clients who could not afford to pay for a CD4 count at the time of ART initiation. This could have introduced a bias since only the richer, who could afford to pay, were selected. The influence of the bias is, however, unlikely to have affected the results since social support still emerged as a significant predictor for delayed ART initiation. The influence of the possible selection bias introduced by only including subjects alive at the time of study, often encountered when using retrospective real-life data, is impossible to determine, but is unlikely to have affected the results for the study since the risk factors such as stock-outs of ARVs for the dead clients are likely to have been the same.

Recall bias

In study IV (case-control) the respondents were asked questions related to several variables of the study that could have occurred at most five years prior. Recall bias generated by this phenomenon is, however, unlikely to have played any major role in this study since the identified risk factors like availability of drugs did not require any detailed retrospective recall that could be assumed to differ between cases and controls subject in this study.

Sampling bias

Some CIs in study IV are wide due to the fairly small sample size. However, the sampled data still allowed us to identify a number of statistically significant predictors for very late initiation of ART with enough precision to lay the groundwork for the necessary health systems and policy interventions needed to encourage earlier ART initiation.

Generalisability and Transferability

The findings of studies II and IV did not include pediatric PLHIV, nor were women identified as HIV+ in PMTCT included in study IV, which limits generalisability to these groups. Quantitative results could be transferred to other rural Ugandan districts and other SSA settings where the health system structures, resource-level and community settings are similar to those of Iganga district. While Iganga district is relatively densely populated, the identified barriers to care may be even stronger in more sparsely populated settings.

For the qualitative studies (I and III), the transferability of our findings to populations and contexts beyond our research context may be more limited. We have, however, tried to give a thick description of the research and analysis process to enable judgements by other readers on how transferable our findings are to other comparable contexts (Dahlgren et al., 2004).

9.0 CONCLUSIONS

- Inadequate post-test counselling due to staff workload and lack of incentive to emphasise the importance of pre-ARV care to newly screened PLHIV hinders uptake and adherence to regular pre-ARV care for non-ART-eligible PLHIV. (I)

- Extended counselling by staff with short-term training in basic counselling skills combined with home visits by volunteer community network support agents for ongoing counselling is associated with uptake of regular pre-ARV care and status disclosure for PLHIV. (II)

- Competition from the influential traditional/spiritual healers, who are perceived by the PLHIV as being accessible, friendly, cheaper, holistic and to offer better-quality services than Government facilities, is a barrier to regular pre-ARV care and timely initiation of ART. (I and III)

- ARV stock-outs, inadequate or lack of pre-ARV care, lack of staff confidentiality, prevailing stigma and lack of social support, and misconceptions about ARVs or their package labels are barriers to timely initiation of ART. (III)

- Lack of pre-ARV care, lack of family/social support, competition from traditional/spiritual healers and ARV stock-outs are crucial risk factors which are significantly associated with very late initiation of ART. (IV)

10.0 POLICY IMPLICATIONS

Findings from the studies outlined in this thesis have implications for policy on uptake of pre-ARV care, loss to follow-up of PLHIV during pre-ARV care, and timely initiation of ART. The basic foundation is that there are already existing policies at national and international level (Uganda National Health Policy, Health Sector Strategic Plan II, the National AIDS Policy and UNAIDS policies) to address the system deficiencies and individual/community factors that influence loss to follow-up during pre-ARV care and timely initiation of ART. The inferences of this thesis are a contemplation of how we can get the policies into practice in the context of our findings.

Practice should highlight recruitment of counsellors or training of staff in the pre-ARV/ART clinic in counselling skills to address inadequate post-test counselling for newly screened PLHIV. This should be complemented by home visits by the network support agents for ongoing counselling to PLHIV. This practice will encourage uptake and reduce loss to follow-up of PLHIV in HIV care, and enhance status disclosure and family social support in the long run.

The influential and accessible spiritual/traditional healers should be considered for sensitisation and integration into pre-ARV care, with close monitoring and support supervision by the government. Such integration has registered some success in HIV counselling and herbal research with regard to managing PLHIV in Uganda and Zambia.

Community network support agents could be trained, supported and supervised for doorstep cotrimoxazole distribution to PLHIV in their homes, as is done with the home-based management of fever. This would reduce transport costs and waiting time for PLHIV. However, the authorities will need to address other important system deficiencies such as stock-outs of HIV testing kits and cotrimoxazole, as well as staff attitudes towards pre-ARV care and the perceived lack of staff confidentiality.

There is a need to ensure that all new HIV clients access regular pre-ARV care for routine monitoring in order to start ART on time. Pre-ARV care should be supplemented with economically viable,

established social support networks for PLHIV, such as post-test clubs with income-generating activities targeting especially the poor and most vulnerable PLHIV.

Policy makers and health care providers must also put more emphasis on strategic ARV procurement planning and the supply chain to prevent stock-outs through appropriate coordination and control of the different stakeholders at national and subnational levels. This could be supplemented by taking ARVs closer to the community to cut access costs, as has been established by studies in Uganda where ART was successfully delivered locally through appropriate training and support supervision of lay workers and lower cadre staff. Making ART services more affordable, accessible and user-friendly through peripheral units could help to make ART centres/services more attractive than traditional healers.

Authorities also need to send out media messages and information, education and communication materials that address resentment of PLHIV, self-stigma and misconceptions about ARVs and their branding, to enhance acceptability of ART by PLHIV. Great care must, however, be taken to pilot the disseminated information, if possible in all the local languages, to make sure it is accurate and to avoid misinterpretation.

Gender inequality, where women lack information about HIV and HIV care in general could be addressed by sensitising women about the importance of HCT and pre-ARV care through the local media and local leaders. Men also need to be sensitized against HIV stigma and the importance of early HIV diagnosis and care.

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